

ROLE OF SERUM MAGNESIUM IN DIABETES MELLITUS: A CASE-CONTROL STUDY**Dr. Chandan Sharma***

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ABSTRACT

Background: Diabetes-Mellitus (DM) is the most common endocrine disorder, encountered in clinical practice. At the same time, micronutrients are known as potential, preventive and therapeutic agents and among them, magnesium merits special attention. Magnesium is essential for insulin secretion, insulin receptor interaction or normal carbohydrate utilization. Therefore, the aim of this study was to analyse serum magnesium levels among diabetes mellitus patients. **Method:** A case-control study was performed on 80 diabetic patients, age >20 years, attending the outpatient Department of Medicine, Government Medical College, Jammu, for a period of 6 months. 40 age-matched healthy controls were also selected for the study. **Results:** Out of 80 Type 2 diabetics, 51.25% were between 40-60 years; 55% were males; 45% were females. Serum magnesium levels among normal healthy controls were 1.92 ± 0.23 mg/dl and 1.56 ± 0.46 mg/dl among cases, with 66.25% patients had mean range of 1.1-2.0 mg/dl. Mean HbA1c among patients was $7.67\% \pm 1.92\%$. Patients with longer duration of diabetes showed highest mean HbA1c values (8.04 %) and lowest mean serum magnesium values (1.36 mg/dl). 35 patients in the study group had one or more macro or micro vascular complications. Thus hypomagnesemia appeared to be an additional risk factor in the development and progression of DM. **Conclusion:** Since, the treatment of the diabetes requires a multidisciplinary approach whereby every potential complicating factor must be monitored and treated. It is advisable to include serum magnesium in the routine electrolyte panel for the better management of diabetes mellitus.

INTRODUCTION

Diabetes-Mellitus (DM) is the most common endocrine disorder, encountered in clinical practice. The worldwide prevalence of diabetes mellitus has risen from an estimated 30 million cases in 1985 to 177 million cases in 2000. It is estimated that more than 360 million individuals will be having diabetes by year 2030^[1] The prevalence of diabetes is higher in the developing countries (6.2% in 2000), than in developed countries (3.5% in 2000).^[2] Among Asian countries, in China for instance, diabetes has reached epidemic proportions, affecting as much as 9.7% of the adult population.^[3] Diabetes is a progressive disorder, therefore complications are inevitable. People with severe hyperglycemia can remain largely asymptomatic for a long period, leading to organ damage by the time it is clinically diagnosed. This leaves an enormous impact of diabetes on morbidity and early mortality. This underscores the importance of closely examining all possible factors in pathogenesis.^[4]

Micronutrients are known as potential, preventive and therapeutic agents for type 2 diabetes mellitus and their complications.^[5] But, the restricted diets which most diabetics must follow do not allow them to meet the recommended daily allowances of micronutrients. DM

has shown to be associated with abnormalities in the metabolism of zinc, magnesium, chromium, copper, and manganese,^[6] out of these, magnesium has been investigated as a clinically significant electrolyte, under new researches.^[7] Magnesium is essential for insulin secretion, insulin receptor interaction or normal carbohydrate utilization (by Mg dependent enzymes). A compromise in these functions leads to insulin resistance in hypomagnesaemia, which is contributed by: Hyperglycemia: leading to decreased cellular Mg levels or by diuresis: either osmotic or due to the use of diuretics and hypolipidemic agents, directly leading to increased urinary Mg losses.^[8,9] Magnesium intake has been found inversely associated with incidence of diabetes among young adults, which can be explained by the inverse correlation of magnesium with their complications like diabetic retinopathy, diabetic nephropathy and diabetic neuropathy.^[10,11]

Hypomagnesaemia may be defined as a serum Mg concentration of ≤ 1.6 mg/dl (normal serum Mg concentration considered; 1.5- 2.5 mg/dl).^[12] Magnesium supplementation is considered safe and effective for the improvement of hypomagnesaemia and hence diabetic complications too. However, no supplements can replace insulin for patients with DM, these supplements may

only reduce need of medications. Hypomagnesaemia has been linked to various micro and macro vascular complications, this makes the better understanding of Mg metabolism in the routine management of diabetes, very important.^[13]

With an eye on universal screening of diabetes for searching out means of early detection and intervention, this study was planned and aimed at finding serum magnesium levels among diabetes mellitus patients.

MATERIAL AND METHODS

A hospital based case-control study was performed on randomly selected 80 diabetic patients attending the outpatient Department of Medicine, Government Medical College, Jammu, for a period of 6 Months. Forty age-matched healthy controls were also selected for the study. Informed and written consent was obtained from all participants.

Inclusion Criteria: Type 2 DM patients, of either gender, age 20 years and above and willing to participate in the study.

Exclusion Criteria: Cases suffering from diabetic

Ketoacidosis, hyperthyroidism, pancreatitis, carcinoma of pancreas, hyperpituitarism or cushing's disease. Patient on medications like phenothiazines, caffeine, nicotine, levodopa, morphine, steroids, oral contraceptives, etc.

Samples were collected 5 ml of venous blood aseptically collected from antecubital vein and the whole blood was put in a vial with no anticoagulant and allowed to stand for some time so that serum was separated for estimation of magnesium levels by Xylidyl blue method where magnesium forms blue violet complex whose intensity is proportional to magnesium concentration in specimen measured at 546 nm.

Data was analyzed using MS Excel 2010 software. Mean and Standard Deviations were found and p-value < 0.05 was considered significant.

RESULTS

Out of 80 Type 2 diabetics, majority of the patients (51.25%) were between 40-60 years; 55% were males and 45% were females. The mean BMI was 26 ± 8.2 among cases and 25 ± 7.4 among controls. (Table 1).

Table 1: Demographic Characteristics of Cases and Controls.

Characteristic	Cases		Controls		P Value	
	N	%	N	%		
Age Group	20-40 Years	31	38.75	15	37.50	0.103
	40-60 Years	41	51.25	21	52.50	
	>60 Years	8	10.00	4	10.00	
Gender	Male	44	55.0	21	52.50	--
	Female	36	45.0	19	47.50	
BMI	Mean \pm SD	26 ± 8.2		25 ± 7.4		--

The serum magnesium levels among normal healthy controls ranged between 1.73- 2.81mg/dl with mean \pm S.D being 1.92 ± 0.23 mg/dl; among diabetic subjects, it

ranged between 0.23- 2.18 mg/dl, with mean \pm S.D being 1.56 ± 0.46 . Of the patients, 23 (28.75%) had low serum magnesium levels of ≤ 1.5 mg/dl. (Table 2) (Table 4).

Table 2: Serum Magnesium levels in patients and normal healthy controls.

Group	Serum Magnesium(mg/dl)		P Value
	Range (mg/dl)	Mean \pm S.D	
Control, n=40	1.73- 2.81	$1.92 \pm 0.23^*$	0.042*
Patients, n=80	0.23- 2.18	$1.56 \pm 0.46^*$	

p<0.05

53 (66.25%) diabetic subjects under study showed serum magnesium levels in the mean range of 1.1-2.0. (Figure 1)

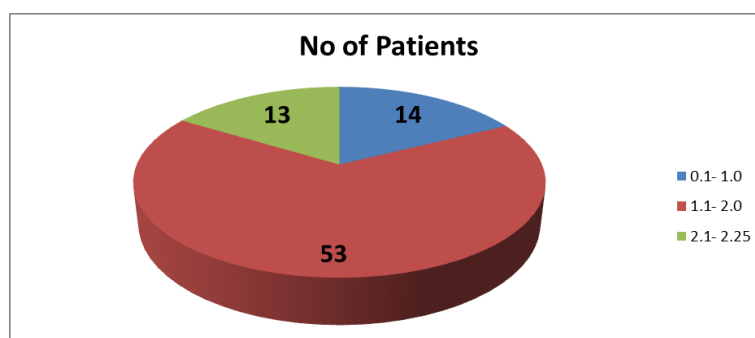


Figure 1: Distribution of type 2 diabetics as per magnesium levels.

HbA1c of 7% or above was considered as poor glycemic control. The mean HbA1c among patients was 7.67% ± 1.92%. The HbA1c value was thus poor among 59/80

(73.75%) patients. There were only 2 patients with HbA1c level ≥10% indicating very poor glycemic control. (Figure 2)

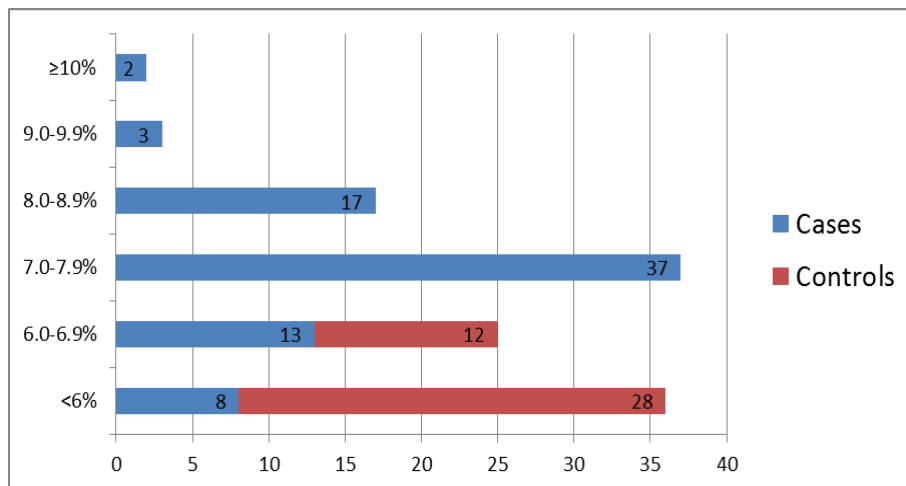


Figure 2: Distribution of HbA1c value of patients and controls.

It was also observed that patients with longer duration of diabetes, here ≥ 10 years, had highest mean HbA1c values (8.04 %) and lowest mean serum magnesium values (1.36 mg/dl). (Table 3)

Table 3: Serum magnesium level in relation to duration of diabetes.

Duration of diabetes	No. of patients	Mean HbA1C (%)	Mean serum magnesium (mg/dl)
< 6 years	34	7.28	1.69
6 to 10 years	20	7.65	1.63
≥ 10 years	26	8.04	1.36

10 patients with diabetes mellitus for less than 6 years had low serum Magnesium. 7 out of 26 patients with diabetes mellitus ≥ 10 years duration had low serum magnesium. (Table 4)

Table 4: Distribution of hypomagnesaemia according to duration of diabetes

Duration of diabetes	Normal Sr. Mg > 1.5 mg/dl	Low Sr. Mg ≤ 1.5 mg/dl	Total
< 6 years	28	6	34
6 to 10 years	15	5	20
≥ 10 years	14	12	26
Total	57	23	80

Table 6: Serum magnesium levels in different age groups.

Age (In years)	Cases		Controls		P- Value
	Numbers	Serum Mg (Mean ± SD)	Numbers	Serum Mg (Mean ± SD)	
20-40	31	1.71 ± 0.32	15	2.2 ± 0.49	0.005*
40-60	41	1.72 ± 0.46	21	2.0 ± 0.53	0.012*
>60	8	1.48 ± 0.56	4	2.0 ± 0.45	0.001*

*p<0.05 = statistically significant

35 patients in the study group had one or more macro or micro vascular complications. Of these 35, 21 patients

We observed that a total of 23 patients had serum magnesium of ≤ 1.5 mg/dl, 57 patients had a higher serum magnesium level. There seems to be an inverse relation between the duration of diabetes and Serum Mg levels. (Table 5)

Table 5: Serum magnesium level according to duration of diabetes.

Serum magnesium Levels (mg/dl)	Number of patients	< 6 years	6 to 10 years	≥ 10 years
≤ 1.5	23	6	5	12
1.6 - 1.7	26	9	10	7
1.8 - 2.0	14	8	3	3
> 2.0	17	11	2	4

It was also observed that maximum number of subjects were found in the age groups of 20 to 40 and 40 to 60 years, with a statistically significant difference between Mean serum magnesium levels of Cases and Controls in all the three age groups. (Table 6)

had single complications, 10 patients had two complications, 2 patients had three complications and 2

had four complications. There were more patients with micro vascular complications like: neuropathy, nephropathy or retinopathy, while coronary artery disease (CAD) was the most common among the macro vascular complications. (Table 7)

Table 7: Distribution of complications among patients.

Complications	Low Mg	Normal Mg	Total
Neuropathy	11	8	19
Nephropathy	6	5	11
Retinopathy	4	6	10
CVA	2	2	4
CAD	8	4	12
PVD	1	0	1

DISCUSSION

Trace elements are required for growth and maintenance of life and health. The clinical significance and evaluation of zinc, copper, chromium, manganese regarding diabetes mellitus may be controversial, but, magnesium has many wider metabolic implications as it relates to diabetes mellitus.

In the present study, the serum magnesium levels among normal healthy controls (n=40) ranged between 1.73-2.81mg/dl with mean \pm S.D being 1.92 ± 0.23 mg/dl; among diabetic subjects (n=80), it ranged between 0.23-2.18 mg/dl, with mean \pm S.D being 1.56 ± 0.46 . The levels of serum magnesium significantly lower in patients as compared to normal healthy individuals.

Thus, the present study confirms the finding that the patients with type 2 diabetes mellitus have significantly lower levels of magnesium as compared to controls as reported by several workers in the previous studies.^[10] It was observed that maximum number of diabetics was in the range of 1.1 to 2.0 mg/dl and most prevalent levels of serum magnesium encountered amongst type 2 diabetics to be 1.56 mg/dl. A similar finding was reported by Young D S et al.^[14]

Maximum numbers of subjects were found in the age groups of 20 to 40 and 40 to 60 years, with a statistically significant difference between Mean serum magnesium levels of Cases and Controls in all the three age groups.

It was also observed that patients with duration of diabetes \geq 10 years, had highest mean HbA1c values (8.04 %) and lowest mean serum magnesium values (1.36 mg/dl). 7 out of 26 patients with diabetes mellitus \geq 10 years duration had low serum magnesium. Longer duration of diabetes is associated with a higher incidence of complications due to the longer duration of uncontrolled diabetic status associated with lower magnesium levels.

HbA1c of 7% or above was considered as poor glycemic control. The mean HbA1c among patients was $7.67\% \pm 1.92\%$ in this study and HbA1c value was poor among

73.75% patients. 53 (66.25%) diabetic subjects under study showed serum magnesium levels in the mean range of 1.1-2.0, which was found to be low. Lima et al.^[15] had also concluded that magnesium depletion is common in poorly controlled patients of type 2 diabetes mellitus. More such studies have suggested an association between magnesium depletion and insulin resistance and/or reduction of insulin secretion in these cases.

The association of low serum magnesium level with single or multiple complications is highly significant as against those without complications. The work done by Grafton et al.^[16] shows that hypomagnesemia causes a decrease in the affinity of the inositol transport protein for inositol, leading to a two-fold reduction in the rate of inositol transport, which further links diabetes and its vascular complications. In our study, out of 35 patients with vascular complications, 21 patients had single complications, 10 patients had two complications and 4 patients had three or more complications. There were more patients with micro vascular complications. Out of 10 patients with diabetic retinopathy, 4 were associated with low serum magnesium. Out of 19 patients with diabetic neuropathy, 11 were associated with low serum magnesium. Thus hypomagnesemia appears to be an additional risk factor in the development and progression of this complication.^[17] These results were also supported by many other studies as well.^[15]

Reduced magnesium concentration in T2DM and hypertensive patients may result in a defective tyrosine-kinase activity at the insulin receptor level and exaggerated intracellular Calcium concentration. This may be responsible for impairment in insulin action and worsening of insulin resistance in non-insulin-dependent diabetes mellitus (NIDDM). Resnik et al.^[18] also proposed that the primary defect present in all organ systems is an abnormality of cellular ion handling.

The limitation of the present study is that the effect of magnesium supplementation on patients and controls was not taken in the direct preview.

CONCLUSIONS

Serum magnesium levels are not investigated in routine clinical practice despite its significance. Hypomagnesaemia is often overlooked while it is being reported to occur with increased frequency among patients with type 2 diabetes mellitus. The treatment of the diabetes requires a multidisciplinary approach whereby every potential complicating factor must be monitored closely and treated. Oral magnesium can restore serum magnesium levels, improving insulin sensitivity and also has the potential to improve some of the diabetic complications. It is therefore advisable to include serum magnesium in the routine electrolyte panel for the better management of diabetes mellitus.

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DECLARATIONS

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