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INSIGHT INTO THE ROLE OF SERUM MAGNESIUM IN GLYCEMIC CONTROL OF TYPE 2 DIABETES MELLITUS

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ABSTRACT

Background: Intracellular magnesium (Mg^{2+}), a macro mineral plays a key role in regulating insulin action. Thus magnesium deficiency can contribute to insulin resistance. In this regard we have studied the serum magnesium levels to know its relationship with type 2 diabetes mellitus (type 2 DM) and also to evaluate its association with the glycemic control. **Materials and Methods:** One hundred and fifty subjects in the age group of 35-60 years attending medical OPD of Rajarajeswari Medical College and Hospital, Bengaluru, were included in the study. Hundred, type 2 DM patients were divided into two groups; group I -consisting of fifty subjects with poor glycemic control and group II- fifty subjects with good glycemic control. Fifty, non-diabetic apparently healthy volunteers were considered as group III. Serum FBS and PPBS was estimated by GOD-POD method, Glycosylated Hemoglobin (HbA_{1c}) by particle enhanced immunoturbidimetric method and Serum Magnesium by Xylidil blue spectrophotometric method. **Results:** Mean serum magnesium level was 1.97 ± 0.43 mg/dl and 2.0 ± 0.22 mg/dl in type 2 DM patients and non-diabetic healthy volunteers respectively. Though there was no significant difference in serum magnesium levels between the three study groups, incidence of hypomagnesemia was high (38%) in diabetic group compared to non-diabetic healthy volunteers (12%). Group I subjects had high incidence of hypomagnesemia (40%) than group II (36%). **Conclusion:** Hypomagnesemia is common among type 2 diabetics irrespective of glycemic control. This incidence is multifactorial and needs further investigation in larger population.

KEYWORDS: Type 2 DM; Serum Mg^{2+}; glycemic control; hypomagnesemia.

INTRODUCTION

Magnesium is second most common intracellular cation and fourth most common cation in the body.[1] It serves as a cofactor in more than 320 enzymatic reactions involving energy metabolism and particularly in insulin action.[2,3] In this regard we have studied the serum magnesium level to know its relationship with type 2 DM and also to evaluate its association with the glycemic control.

MATERIALS AND METHODS

A total of one hundred and fifty subjects in the age group of 35-60 years attending medical OPD of Rajarajeswari Medical College and Hospital, Bengaluru were included in the study. Hundred, diabetic patients were divided into 2 groups with 50 subjects each; group I consisting of type 2 DM patients with poor glycemic control (HbA_{1c} ≥7.0 %), group II consisting of type 2 DM patients with good glycemic control (HbA_{1c} <7.0 %) and non-diabetic apparently healthy volunteers were considered as group III. Type 2 DM patients with history of renal failure, cirrhosis of liver, alcoholism, cancer and other medical and surgical illness were excluded from the study.

After obtaining Institutional ethical clearance, informed consent was taken from all the study subjects. Under full aseptic precautions, 5ml of venous blood was collected in fasting state and 2ml in post prandial state. Clot activator tubes were used for estimation of serum magnesium and fluoride EDTA tubes for estimation of blood glucose and glycosylated hemoglobin.

FBS and PPBS was determined by glucose-oxidase peroxidase method in fully automated Mindry BS 300 analyzer (kits supplied by Mindry). Glycosylated

Hemoglobin (HbA_{1c}) was estimated by particle enhanced immunoturbidimetric method (kits supplied by Mindray). HbA_{1c} is determined directly without measurement of total hemoglobin. Principle: Total hemoglobin and HbA_{1c} in hemolysed blood bind with the same affinity to particles in latex buffer. The amount of binding is proportional to the relative concentration of both substances in the blood. Mouse anti-human HbA_{1c} monoclonal antibody binds to particle bound HbA_{1c}. Goat anti-mouse IgG polyclonal antibody interacts with the monoclonal mouse anti-human HbA_{1c} antibody and agglutination takes place. The measured absorbance is proportional to the HbA_{1c} bound to particles, which in turn is proportional to the percentage of HbA_{1c} in the sample. Expected range: Nondiabetic: 4.0-6.0%, good control: <7%, poor control: >7.0%. Serum magnesium was estimated by Xylidil blue spectrophotometric method (Accucare kits). Magnesium in the serum reacts with Xylidil blue to form a colored compound in alkaline solution.

STATISTICS

This is a descriptive study. The data obtained was analyzed statistically using One way Anova calculator for independent measures. Pearson's correlation coefficient was used to find out the correlation.

RESULTS

One hundred and fifty subjects in three groups were studied. We observed equal number of male and female subjects with average age of 45-55 years in each study group (table No.1).

Table No. 1: Age distribution among cases and controls.

Age in Years	Type II DM		Non-diabetic healthy volunteers
	Group I (Poor glycemic control) HbA_{1c} >7mg/dl	**Group II** (Good glycemic control) HbA_{1c} <7mg/dl	**Group III**
30-39 Years	13	06	15
40-49 years	11	12	10
50-59 years	09	12	12
60-70 years	17	20	13
Total Study subjects	50	50	50

Mean FBS and PPBS levels in three study groups was as follows (table No. 2). There was significant difference in FBS, PPBS and HbA_{1c} levels among the three study groups at p<0.001.

Table No. 2: FBS and PPBS among the study groups.

Parameters	Type II DM		Non-diabetic healthy volunteers
	Group I	**Group II**	**Group III**
FBS	204.54 ± 77.04	127.82 ± 45.05	86.78
PPBS	310.7 ±83.36	208 ± 80.96	121.02
HbA_{1C}	8.179 ± 0.89	6.078 ± 0.639	5.21 ± 0.27

Mean serum magnesium level in hundred type 2 DM patients and fifty non-diabetic healthy controls was 1.97 ± 0.43 mg/dl and 2.05 ± 0.22 mg/dl respectively. Mean serum Mg^{2+} levels in group I and II with *p* values are as follows (table No. 3).

Table No. 3: Serum magnesium levels among the three study groups.

	Type II DM	Healthy volunteers (50 subjects)	*p* value
Serum Mg^{2+} levels in mg/dl Mean ± SD	(All 100 type 2 DM subjects) 1.972 ± 0.43	2.05	0.88
	Group I (50 subjects) 1.96 ± 0.43		0.35
	Group II (50 subjects) 1.98 ± 0.43		0.22
	Group I and II		0.79

p value >0.1 not significant, *p* <0.05 moderately significant, *p*<0.001 highly significant

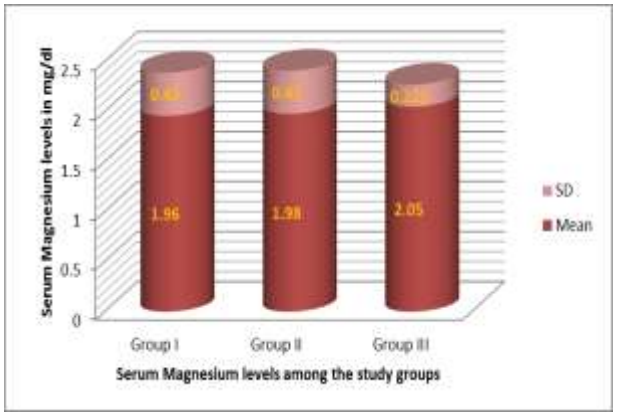

Figure No. 1: Bar diagram depicting serum Magnesium level among the three study groups.

Serum Mg^{2+} was in the lower limit of reference range (1.9-2.5mg/dl) in both the diabetic groups. Even though there was no significant difference in serum magnesium level among the study groups, high incidence (38%) of hypomagnesemia (serum Mg^{2+} < 1.9mg/dl) was observed in diabetics compared to healthy volunteers (12%). Incidence of hypomagnesemia was high in group I (40%) subjects compared to group II (36%) subjects. (Refer figure No. 2).

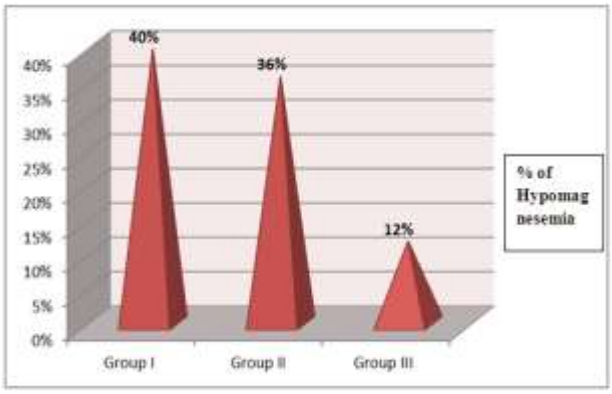

Figure No. 2: Incidence of Hypomagnesemia among the three study groups.

Mean serum Mg^{2+} was calculated in subjects with hypomagnesemia in all the three groups (table No. 4).

Table No. 4: Serum magnesium levels among the Hypomagnesemia patients of the three study groups.

	Group I	Group II	Group III
No. of patients with hypomagnesemia	20	18	6
Serum Mg2+ levels (Mean ± SD in mg/dl)	1.54 ± 0.27	1.58 ± 0.24	1.7 ± 0.014

Even in subjects with hypomagnesemia, there was no significant difference in serum magnesium levels among the three study groups.

The Pearson correlation co-efficient is used to measure the strength of a linear association between two variables, where the value r = 1 means a perfect positive correlation and the value r = -1 means a perfect negative correlation. The value nearer to the zero, weaker is the relationship.

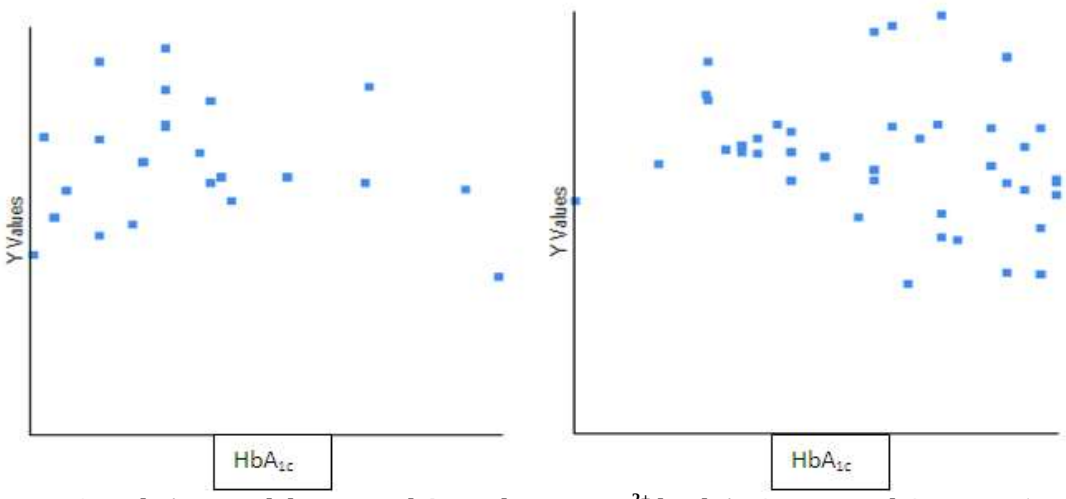

Figure No. 4: Correlation graph between HbA_{1c} and serum Mg^{2+} levels in Group I and Group II. (Variables: X = HbA_{1c} values, Y = serum Mg^{2+} values).

A weak negative correlation was observed between HbA_{1c} and serum Mg^{2+} level among the two diabetic groups with r = - 0.0726 and r = - 0.2387 respectively.

A weak negative correlation was observed between HbA_{1c} and serum Mg^{2+} level even in subjects with hypomagnesemia of two diabetic groups with r = - 0.2684 and r = - 0.1953 respectively.

DISCUSSION

Type 2 diabetes mellitus and its complications are increasing alarmingly worldwide. Hence the disease has to be treated meticulously, considering every potential complicating factor. Type 2 DM is characterized by insulin resistance and relative insulin deficiency.

Intracellular magnesium (Mg^{2+}), a macro mineral plays a key role in regulating insulin action[4] and in glucose uptake via insulin receptor mediated tyrosine kinase activity.[5,6] In addition Mg^{2+} is a cofactor for several enzymes of carbohydrate metabolism. Magnesium deficiency thus contributes to insulin resistance. Impaired metabolism of Mg^{2+} may have a contributory role in the progression of DM and its complications.[7,8,9,10,11]

In this study, mean serum Mg^{2+} level was within the reference range in all the three study groups and the serum Mg^{2+} level among the diabetics was towards the lower limit of the reference range. Though there was no significant difference in serum Mg^{2+} level among the three study groups, we observed high incidence of hypomagnesemia in type 2 DM patients (irrespective of the glycemic control) compared to non-diabetic healthy volunteers. Hypomagnesemia has been reported to occur with increasing frequency among diabetics.[12] The reasons for magnesium deficiency in diabetes are not very clear. This could be due to higher urinary loss (glomerular hyperfiltration) and lower dietary intake/impaired absorption.[13] In addition, increased gastrointestinal loss as a result of autonomic dysfunction, osmotic diuresis due to glycosuria,[14,15] hereditary factors, altered insulin metabolism, recurrent metabolic acidosis, hypophosphataemia, hypokalaemia,[16,17] concomitant use of diuretics and hypolipidemic drugs[18] may all contribute to hypomagnesaemia in diabetic patients. Renal function is said to be the major regulator of the serum Mg^{2+} level.[19] Rude R K et al in his study says that approximately one-third of patients with type 2 diabetes have hypomagnesemia, mainly caused by enhanced renal excretion.[20]

Similar to our study findings, few authors[13,21,22,23,24] found no significant difference in serum magnesium level in diabetic patients as compared to controls. Contrary to our findings, majority of the researchers[25,26,27,28] observed statistically significant decrease in serum Mg^{2+} levels in diabetics. This observation may be due to differences in the selection of the study subjects like socioeconomic status, duration of the disease, glycemic control. Literature search shows that hypomagnesemia is linked to poor control of type 2 diabetes mellitus and depletion of serum magnesium occurs exponentially with duration of disease[29] and also magnesium supplementation improves insulin sensitivity.[30]

Though there was no significant difference in serum magnesium levels among group I and II, we observed hypomagnesemia in 40% of subjects in group I and 36% of subjects in group II. Even among these subjects we did not observe significant difference in the serum magnesium levels, but we observed a weak negative correlation between HbA_{1c} and serum magnesium level.[31]

Whether hypomagnesemia is a cause or consequence of diabetes is still debatable, but literature search reveals that it contributes to the development and progression of diabetic complications.[7,8,9,10,11] Hypomagnesemia is potential cause of hypocalcemia in diabetics.[32] Unlike hypomagnesemia, hypocalcemia is well recongnized and treated condition in clinical practice. Since 'Mg^{2+} is natures physiologic calcium blocker';[33] (intracelluclar magnesium blocks the entry of calcium ions in to the cells but in hypomagnesemia calcium ions enters in resulting in hypocalcemia) hypomagnesemia has to be corrected first instead of hypocalcemia. Considering all these factors, serum Mg^{2+} should be monitored routinely and hypomagnesemia should be treated promptly to prevent the diabetes related complications.

CONCLUSION

Hypomagnesemia is common among type 2 diabetics, irrespective of glycemic control. This incidence is multifactorial and needs further investigation in larger population. It may be judicious in clinical practice to do routine surveillance and regular monitoring of serum magnesium to delay the complications associated with it.

LIMITATION OF THE STUDY

It is a cross sectional study with small sample size.

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