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Serum Magnesium Level As A Predictor Of Micro & Macro Vascular Complications Of Type 2 Diabetes Mellitus And Its Relation To Atherosclerosis

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Abstract: ***Background:*** *Diabetes Mellitus is a common condition; it causes symptoms that reduces the functional capacity of the bodily systems & negatively affects the quality of life. The risk of atherosclerosis & other forms of diabetic complications increases with reduced levels of serum Magnesium. So, we have designed the study to see the effect of serum magnesium levels on micro & macro vascular complications of Diabetes Mellitus & its relation to atherosclerosis.* ***Material & Methods :*** *A CASE CONTROL study was done, in which subjects with DM type 2 attending medicine OPD and admitted in Mahatma Gandhi Medical College were taken as cases also of age group above 30 years.* ***Results :*** *In our study showed that the mean age was 51 years of cases and male to female ratio was 2.12:1. The microvascular complication such as diabetic retinopathy, neuropathy & nephropathy was 26%, 18% & 22% cases present with hypomagnesemia (<1.8mg/dl) and 14%, 20% & 12% present with normomagnesemia (1.8-2.5 mg/dl).*
The macrovascular complication such as MI,PVD & CVA was 16%, 14% & 14% cases present with hypomagnesemia (<1.8mg/dl) and 6%, 4% & 2% present with normo-magnesemia (1.8-2.5 mg/dl).
The mean serum magnesium levels in patients with HbA1c levels ≥ 8.5% were significantly low (1.561±0.38 mg/dL) compared to patient with HbA1c levels 6.5 to 6.99% . ***Conclusion :*** *There was a strong correlation between hypomagnesemia and microvascular complications (diabetic retinopathy, nephropathy and neuropathy). Hypomagnesemia may be an independent risk factor responsible for the development of microvascular and macrovascular complications, to prove, further studies may be required.*
Key Words : *Diabetes Mellitus, Atherosclerosis, Serum Magnesium*

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I. Introduction:

Diabetes mellitus lead to impaired metabolism of carbohydrates, proteins, fats, water and electrolytes. The sequel of diabetes mellitus was long term damage and failure of multiple organs such as kidneys, nerves, eyes, heart and blood vessels. Several different types of diabetes mellitus were caused by composite interaction of hereditary and geographical factors.[1]

The incidence of diabetes is increasing rapidly at an alarming rate.[2] It is important to note that the increase prevalence is seen in all six inhabited continents worldwide.[3] Over the last 30 years, the estimation of diabetes was changed from being appraise as a mild disease of the old age to one of the major causes of mortality affecting the young and middle aged people.

Globally the number of diabetic patients expected to raise 11.4% from 366 million in 2011 to 552 million by 2030, affecting one in every 10 adults[4]. According to the IDF (International Diabetes Foundation), the diabetes recently affected> 62 million Indians, which is >7.1% of the adult population.[5] The mean age of onset is 42.5 years. Nearly 1 million people die every year in India due to diabetes.[6]

Micronutrients have been explored as a probably preventive and curative agents for T2DM and its complications.[7] In particular, irregular metabolism of Zn, Cr, Cu, magnesium and Mn is associated in diabetes mellitus.[8] Out of these micronutrients, serum magnesium has been identified as clinically, for a long term worldwide strategy to lower the load of diabetes mellitus, with new findings and researches.[9]

Magnesium is the fourth most plentiful electrolyte and the second most plentiful cation intracellularaly in the human body.[10] It has important role in carbohydrate metabolism and is a cofactor for all enzymatic counteraction which needs enzyme kinases.[11] It has pivotal role in enzymatic activation for regulation of ion channel, mitochondrial function, cellular multiplication and apoptosis. It is a necessary factor for both cellular and humoral immunity.[12] Magnesium reduction has a negative effect on glucose eqilibrium and insulin sensitivity in patients with T2DM as well as on the rise of complications such as arterial atherosclerosis,

retinopathy and nephropathy. Furthermore hypomagnesemia is a strong, independent predictor of evolution of microvascular complications in T2DM.[13] Till date, only few studies have evaluated the association of serum magnesium levels with the microvascular & macrovascular complications especially in India. Hence, this study was planned to assess the serum magnesium levels in type 2 DM in patients and to correlate them with the microvascular & macrovascular complications.

II. Material & Methods:

A CASE CONTROL study was done, in which subjects with DM type 2 attending medicine OPD and admitted in Mahatma Gandhi Medical College were taken as cases also of age group above 30 years.

Inclusion criteria:

- All the newly diagnosed patients with type 2 diabetes mellitus between the age group of 30-70 years.
- All diagnosed cases of diabetes mellitus type 2.

Exclusion criteria:

1**.** All type 1 diabetes patients including gestational diabeties .
2. Alcoholics.
3. Patients with drug induced hyperglycaemia.
4. Patients with pancreatitis.
5. Drugs causing Hypomagnesaemia.

Presence of diabetes mellitus was defined as per Indian Diabetes Federation [IDF] Criteria (2011).

Dyslipidaemia as per NCEP ATP III and IDF guidelines
Total cholesterol > 200mg/dl
Triglyceride >150mg/dl
HDL <40mg/dl
LDL >100mg/dl

III. Results:

In our study showed that the mean age was 51 years of cases and male to female ratio was 2.12:1 (table 1). The clinical and biochemical profile of the study population is as shown in table 2.

The microvascular complication such as diabetic retinopathy, neuropathy & nephropathy was 26%, 18% & 22% cases present with hypomagnesemia (<1.8mg/dl) and 14%, 20% & 12% present with normomagnesemia (1.8-2.5 mg/dl) (table 3).

The macrovascular complication such as MI,PVD & CVA was 16%, 14% & 14% cases present with hypomagnesemia (<1.8mg/dl) and 6%, 4% & 2% present with normo-magnesemia (1.8-2.5 mg/dl). (Graph 1)

The mean serum magnesium levels in patients with HbA1c levels ≥ 8.5% were significantly low (1.561±0.38 mg/dL) compared to patient with HbA1c levels 6.5 to 6.99% (1.625 ± 0.67mg/dL). This difference was statistically non significant (p=0.3314) (table 4).

IV. Discussion:

In this study the commonest age group for type 2 DM was more than 41-60 years which comprised of 62% of the patients. The mean age was 51 years of cases. The findings show that diabetes mellitus was widely prevalent among older age. The higher incidence of diabetes among aged can be explained by the increase in the segment of elderly population.[14]

In present study we found that the mean serum magnesium levels in patients with HbA1c levels ≥ 8.5% were significantly low (1.561±0.38 mg/dL) compared to patient with HbA1c levels 6.5 to 6.99% (1.625 ± 0.67mg/dL). This difference was statistically non significant (p=0.3314). These findings hypothesize that, there is reduction of serum magnesium levels with poor diabetic control patients significantly.

Dasgupta A. et al[15] observed remarkebly lower glycemic control in the hypomagnesemia patients as compared to patients with the normal serum magnesium level .

Magnesium is a cofactor of mechanisms of glucose transporting in cell membrane and various enzymatic reaction for oxidation of carbohydrate.[16] In addition, magnesium deficiency has been shown to encourage insulin resistance in multiple studies. Nadler et al. (1995)[17] have stated that sensitivity of insulin reduces in non-diabetic persons after liberate deficiency of magnesium. Like wise, in older patients were represent to have enhance glucose tolerance when they received supplements of magnesium. Thus hypomagnesaemia by itself results in poor glycemic control.

In this study higher number of patients with serum magnesium levels < 1.8 mg/dL had diabetic retinopathy (26%; p=0.1588).

McNair P et al (1978)[18] & Hatwal A et al (1989)[19] found that there is inverse correlation of low serum magnesium level with the degree of retinopathy.

Fujii et al.(1982)[20] who found a marked reduction of magnesium levels in plasma and red blood corpuscles in diabetic retinopathy. Although the theory of depletion in the rate of inositol transport has been proposed by Grafton et al.[21] as a possible mechanism to explain the association between diabetic retinopathy and hypomagnesemia, the exact reason remains unclear.

In the present study frequency of diabetic neuropathy was 18% present in patients with serum magnesium levels < 1.8 mg/dL (p=0.7716). Very few studies have found that level of intracellular magnesium was lower in patients with diabetic neuropathy.[22] Most studies have reported a comparable presence of neuropathy in patients with hypomagnesemia and normomagnesemia. In contrast Dasgupta A., et al.(2012)[15] found that neuropathy was approximate in both groups (82.35% vs 82.70%).

In the present study frequency of MI, PVD & CVA was 16%, 14% & 14% respectively and was higher in patients with serum magnesium levels < 1.8 mg/dL.

Abdul Wahid et al (2017)[23] found that diabetic nephropathy, neuropathy, hypertension and IHD were also higher in hypomagnesemic diabetics as compared to normomagnesemic diabetics, but insignificant.

Resnick et al. (1988)[24] observed that the mean intracellular magnesium concentration was lower in hypertensive patients. Similarly, based on data from the Atherosclerosis Risk in Communities (ARIC) Study, done on middle-aged adults and found that reverse relation between serum magnesium and the risk for coronary heart disease was found among men with diabetes.[72]

V. Conclusion:

We concluded that hypomagnesemia is widely prevalent (50%) among patients with type 2 diabetes mellitus and lower serum magnesium was seen in patients with poor glycemic control and longer duration of diabetes.

There was a strong correlation between hypomagnesemia and microvascular complications (diabetic retinopathy, nephropathy and neuropathy). Hypomagnesemia may be an independent risk factor responsible for the development of microvascular and macrovascular complications, to prove, further studies may be required.

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Table 1: Age & gender wise distribution of cases

Age distribution (years)	Number	Percentage
30-40 years	10	20%
41-50 years	18	36%
51-60 years	13	36%
61-70 yrs	9	18%
Total	50	100%
Gender		
Male	34	68%
Female	16	32%
Male : Female	2.12:1	

Table 2: Characteristics of study population

Parameters	Mean± SD	Range
BMP	24.29±3.556	18.70-31.30
SBP	140.1±19.14	110-184
DBP	90.44±16.09	60-138
HbA1c	9.280±2.220	6.7-14
Hb. (gm/dl)	12.10±1.325	8.2-14.20
TC	212.6±49.49	133-320
TG	193.3±40.06	117-304
LDL	102.4±35.12	60-209
HDL	29.82±7.444	19-45
Serum Creatinine (mg/dl)	1.328±0.6728	0.5-4.7
Urine albumin	494.4±614.5	16-3000
Serum Magnesium (mg/dl)	1.640±0.059	0.5-2.6

Table 3: Association of serum magnesium level with Microvascular complication

Microvascular complications	Serum Magnesium (mg/dl)		Total
	<1.8	1.8-2.5	
Diabetic Retinopathy	13 (26%)	7 (14%)	20 (40%)
Diabetic Neuropathy	9 (18%)	10 (20%)	19 (38%)
Diabetic Nephropathy	11 (22%)	6 (12%)	17 (34%)

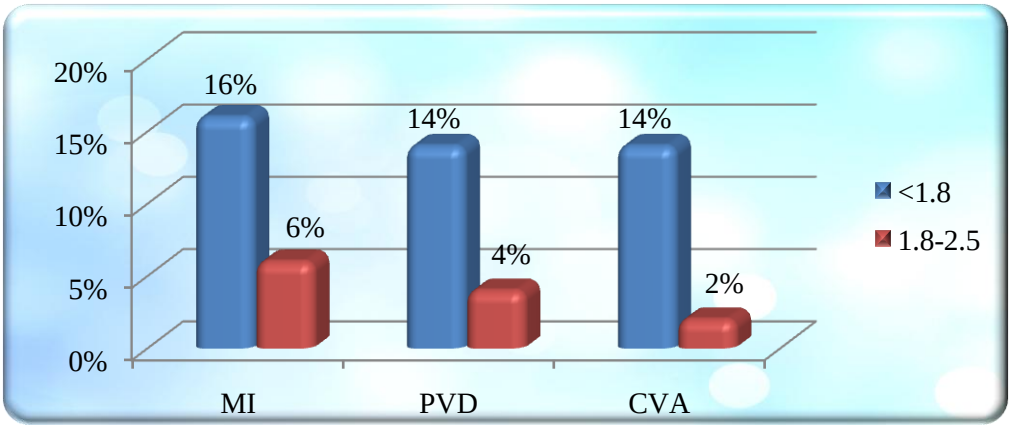

Table 4: Comparison of mean of serum magnesium level with HbA1c

HbA1c (%)	Total	Serum magnesium (mean± SD)	P-value
6.50 to 6.99	4	1.625±0.6702	0.3314
7.00 to 8.49	20	1.615±0.4368	
8.50 to 9.49	8	1.888±0.28	
>9.5	18	1.561±0.3867	

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