Original Research

Study of relation between Serum Magnesium Levels and Vascular Complications in Patients of Type 2 Diabetes Mellitus

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ABSTRACT:
Introduction: Magnesium plays a very important role in the development of type 2 diabetes. Evidence presented for the etiology of type 2 diabetes mellitus does not permit the disease to be considered as an independent entity. Type 2 Diabetes Mellitus patients can have microvascular complications like retinopathy, nephropathy and neuropathy. **Aims & objectives:** To correlate between serum magnesium levels and vascular complications in patients of type 2 Diabetes Mellitus. **Materials and methods:** 50 patients of type 2 diabetes mellitus with micro vascular complications and 50 patients of type 2 diabetes mellitus without micro vascular complications were studied and compared. **Results**: Significant correlation was present in between low magnesium levels and microvascular complications. **Conclusion**: It is important to regularly monitor magnesium levels in all type 2 Diabetic patients. Because magnesium depletion reduces insulin sensitivity and may increase risk of secondary complications, it may be prudent in clinical practice to periodically monitor plasma magnesium concentrations in diabetic patients.
Key words: Diabetes mellitus, nephropathy, neuropathy, retinopathy, serum magnesium.

INTRODUCTION:
The term Diabetes Mellitus, (derived from greek words meaning - siphon and sweet) is a heterogeneous group of metabolic disorders characterized by chronic hyperglycemia with disturbance of carbohydrate, fat and protein metabolism resulting from defects in insulin secretion, insulin action or both.[1,2] Type 2 diabetes accounts for approximately 90 to 95% of all diagnosed cases of diabetes.[3] Studies suggest that at the time of diagnosis, the typical patient with type 2 Diabetes Mellitus have diabetes for at least 4 to 7 years.[4] The precise mechanism for development of microvascular changes is not fully understood, it is possible that hypomagnesaemia inhibits prostacyclin receptor function producing an imbalance between prostacyclin and thromboxane effect which has marked atherogenic potential which is responsible for microvascular complications.[5]

Hypomagnesaemia is a common feature in patients with type 2 diabetes. Although diabetes can induce hypomagnesaemia, magnesium deficiency has also been proposed as a risk factor for type 2 Diabetes Mellitus.[2]

Minimal work has been done in this sphere in our setup. The present study was undertaken to correlate between serum magnesium levels and vascular complications in patients of type 2 Diabetes Mellitus. The findings of the study will help in better management of Diabetes Mellitus in future.

MATERIALS AND METHODS:
This open, prospective, observational, comparative study was conducted in Department of Medicine, Guru Nanak Dev Hospital, Amritsar after taking approval from Institutional Ethics Committee, Government Medical College, Amritsar. The study included 100 patients (50 Cases + 50 Controls) in age group 20-85 years attending outdoor and indoor patient department in Guru Nanak Dev Hospital, Amritsar diagnosed as diabetes mellitus ruled out by random blood sugar and fasting blood sugar. Study group consisted of 50 patients of type 2 diabetes mellitus with micro vascular complications. Control group consisted of 50 patients of type 2 diabetes mellitus without micro vascular complications. All cases of type 2 diabetes mellitus taken for the study were between age group of 20 to 85 years. Random blood sugar and fasting

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blood sugar was checked and 12 lead Electrocardiogram were taken for all study participants. Serum magnesium was done in all patients. Biochemical tests including liver and renal function tests were performed. These include serum bilirubin, total serum protein (TSP), differential serum protein (DSP), aspartate aminotranferase (SGOT), alanine aminotransferase (SGPT), alkaline phosphatase (ALP), blood urea and serum creatinine. Fundoscopy was done in all patients.

RESULTS:

Table 1: MEAN AGE

	STUDY GROUP (N=50)	CONTROL GROUP (N=50)
Mean Age (in years) ±SD	57.42 ± 12.77981	55.84 ± 12.05547

TABLE 2: SEX DISTRIBUTION

SEX	STUDY GROUP (N=50)	CONTROL GROUP (N=50)
MALES	22	17
FEMALES	28	33
TOTAL	50	50

TABLE 3: level of SBP, DBP, FBS, Hb, TLC, UREA, CREATNINE, Na, K, SGOT, SGPT and Hba1C in both the groups

PARAMETER		NUMBER OF PATIENTS	MEAN	S.D	T VALUE	P VALUE
SBP	STUDY GROUP	50	114.52	8.61	0.8	0.41
	CONTROL GROUP	50	115.96	9.01		
DBP	STUDY GROUP	50	73.86	8.69	0.86	0.39
	CONTROL GROUP	50	75.2	6.7		
FBS	STUDY GROUP	50	214.06	76.62	2.17	0.03
	CONTROL GROUP	50	183.36	64.22		
Hb	STUDY GROUP	50	9.71	2.09	0.70	0.48
	CONTROL GROUP	50	9.42	2.03		
TLC	STUDY GROUP	50	7510	1758	0.63	0.52
	CONTROL GROUP	50	7756	2122		
UREA	STUDY GROUP	50	34.36	17.18	7.8	0.0001
	CONTROL GROUP	50	13.64	7.22		
CREATININE	STUDY GROUP	50	2.35	2.21	0.07	0.94
	CONTROL GROUP	50	2.32	1.95		
SODIUM	STUDY GROUP	50	138.72	10.31	1.1	0.27
	CONTROL GROUP	50	136.94	4.83		
POTASSIUM	STUDY GROUP	50	4.29	1.03	1.34	0.18
	CONTROL GROUP	50	4.06	0.63		
SGOT	STUDY GROUP	50	36.7	7.98	0.04	0.96
	CONTROL GROUP	50	36.592	16.64		
SGPT	STUDY GROUP	50	34.4	7.57	1.33	O.18
	CONTROL GROUP	50	37.02	11.62		
HbAIC	STUDY GROUP	50	8.24	0.60	0.97	0.33
	CONTROL GROUP	50	8.26	0.90		

Systolic blood pressure: SBP, Diastolic blood pressure: DBP, Fasting blood sugar: FBP, Hemoglobin: Hb, Total leucocyte count: TLC, Serum glutamic oxaloacetic transaminase: SGOT, Serum glutamic pyruvic transaminase: SGPT

TABLE 4: SERUM MAGNESIUM LEVEL

	STUDY GROUP (N=50)	CONTROL GROUP(N=50)
MEAN Mg level ±SD	1.22 ± 0.48	1.73 ± 0.53

TABLE 5: MAGNESIUM LEVELS IN MICROVASCULAR COMPLICATIONS

	NEPHROPATHY	NEUROPATHY	RETINOPATHY
MEAN Mg level ±SD	1.22 ± 0.51	1.24 ± 0.44	1.2 ± 0.42

TABLE 5: Correlation between Serum Magnesium and microvascular complications

Microvascular complication		Hypomagnesemia <1.3	Normal Magnesium 1.3 to 2.5	Total	P VALUE
Diabetic nephropathy	PRESENT	20	15	35	0.01
	ABSENT	14	1	15	
Diabetic neuropathy	PRESENT	19	11	30	0.025
	ABSENT	15	5	20	
Diabetic retinopathy	PRESENT	11	1	12	0.043
	ABSENT	23	15	38	

DISCUSSION:

In the present study we included two groups. In study group 50 cases of patients having type 2 diabetes mellitus with micro vascular complications were included and in Control group 50 patients having type 2 diabetes mellitus without micro vascular complications were included.

In our study Mean age of patients for study group is 57.42 years and for control group is 55.84 years. The two-tailed P value equals 0.5261. By conventional criteria, this difference is considered to be not statistically significant. In a similar study done by Prabhu R and Kunche S they reported the mean age of patients as 56.82 and 59.02 years.[6]

In our study there were 22 males and 28 females in study group, 17 males and 33 females in control group. In both the groups females were more than males but this difference was not significant with the p-value = 0.305. In the study done by Prabhu R and Kunche S males were more than females in both the groups which was not in accordance with our study. In their study there were 16 males and 9 females in study group, 15 males and 10 females in control group.[6]

In our study the mean values of HbA1C are 8.24 ± 0.60 and 8.26 ± 0.90 respectively in Group I and Group II. These values are almost similar with the study done by Prabhu R and Kunche S who measured average HbA1C (%) values as 8.98 ± 2.26 and 9.93 ± 2.50 in both groups in their study.[6]

In our study the fasting blood sugar levels in study group and control group are 214.06 mg/dl ± 76.62 and 183.36 mg/dl ± 64.2. FBS is higher in study group as compared to control group. The p value is 0.03 and results are significant. Similar statistically significant results have been reported by Vidya B et al in their study.[7] Supriya et al in their study also showed that FBS in their control group was 81.96 mg/dL and 218.62 mg/dL in case group.[8] The difference in our study and studies done by

them is that the control group is healthy volunteers but in our study its diabetic patients without any microvascular complication. Prabhu R and Kunche S don't found any significant difference in FBS levels which is not in accordance with our study.[6] The reason for this might be the diet of the patient. Most of the diabetics could probably be under strict diabetic diet and some are not.[8]

In our study we found that diabetics with micro vascular complications had significantly lower level of serum magnesium (1.22 ± 0.48) compared to diabetics without micro vascular complications (1.73 ± 0.53). Mean serum magnesium levels in nephropathy neuropathy and retinopathy were 1.22 ± 0.51 mg/dl, 1.24 ± 0.44 mg/dl and 1.2 ± 0.42 mg/dl respectively. These findings are in concordance with Studies done by Baig MSA et al, Dasgupta A et al and Prabhu R and Kunche S.[5,6,9] The reasons for the high prevalence of magnesium deficiency in diabetes are not clear, but may include increased urinary loss, due to osmotic diuresis, lower dietary intake and rampant use of loop and thiazides diuretics promoting magnesium wasting, diabetic autonomic neuropathies, impaired absorption of magnesium compared to healthy individuals. Recently a specific tubular defect in magnesium reabsorption in thick ascending loop of Henle is postulated. This defect results in reduction in tubular reabsorption of magnesium and consequently hypomagnesemia.[10]

Baig MSA et al and Suarez A et al have stated that although the binding of insulin to its receptor does not appear to be altered by magnesium status, the ability of insulin once bound to receptor to activate tyrosine kinase is reduced in hypomagnesaemia states. As a result reduced peripheral glucose uptake and oxidation are often noted in subjects with hypomagnesaemia.[5,11]

Thus hypomagnesaemia may be a possible risk factor in development and progress of diabetic complications. The precise mechanism for development of micro vascular changes is not fully understood, it is

possible that hypomagnesaemia inhibits prostacyclin receptor function producing an imbalance between prostacyclin and thromboxane effect which has marked atherogenic potential which is responsible for micro vascular complications.[5] Some studies have shown that oral supplementation with magnesium chloride solution restores serum magnesium levels improving insulin sensitivity and metabolic control in type 2 diabetic patients with decreased serum magnesium levels.[12]

In our study among the patients with diabetic nephropathy, 21 patients had low serum magnesium levels and 15 patients had normal magnesium levels. There was a statistically significant correlation present (p<0.05). Our observations revealed a definite association between diabetic nephropathy and lower serum magnesium levels. A study by Sajjan NB et al reported that serum levels of Magnesium showed statistically significant difference when compared in healthy subjects & subjects with Diabetic nephropathy.[13] Recently, Dasgupta A et al reported that, both microalbuminuria and macroalbuminuria were found at a higher incidence in the hypomagnesemia group compared with the normomagnesemia group.[9]

The prevalence of diabetic neuropathy is generally is estimated to be 10% to 50% in patients with T2DM, and the incidence increases with age and duration of Diabetes Mellitus.[14,15,16] A nationwide survey performed in 2006 by the Committee of the Korean Diabetes Association on the Epidemiology of Diabetes Mellitus (n=5,652) showed that the prevalence of DPN defined by neurologic symptoms or nerve conduction velocity abnormalities was 44.7%.[10]

Among the patients with diabetic neuropathy, 19 patients had low serum magnesium levels and 11 patients had normal magnesium levels. There was a statistically significant correlation present (p<0.05). In the present study a definite association between diabetic neuropathy and lower serum magnesium levels with significant difference in the prevalence of hypomagnesemia among the patients with neuropathy was noted.

In contrast Dasgupta A et al reported that, neuropathy was comparable in both groups.[9] Very few studies have found that intracellular magnesium levels are lower in patients with diabetic peripheral neuropathy.[14] Most studies have reported a comparable presence of neuropathy in patients with hypomagnesemia and normomagnesemia. In contrast, our study revealed a significantly high prevalence of hypomagnesemia in patients of diabetic neuropathy. Magnesium is known to be necessary for nerve conduction. Deficiency of magnesium increases insulin resistance which is known to affect nerve conduction.[17] This could be one of the mechanisms to define the association of hypomagnesemia and neuropathy in our study.

Among the patients with diabetic retinopathy, 11 patients had low serum magnesium levels and 1 patient had normal magnesium levels. There was a statistically significant correlation present (p<0.05). There was a significant difference in prevalence of hypomagnesemia in diabetics with and without retinopathy Recently,

Dasgupta A et al reported higher incidence of retinopathy in the hypomagnesemia group (64% vs 45.8%).[9] The existence of a close relationship between impaired magnesium balance and retinopathy was established by Fujiiet al who found a marked depletion in plasma and erythrocyte magnesium levels in diabetic patients with advanced retinopathy.[18]

This study reveals a strong association between hypomagnesemia and microvascular complications. Hence it could be suggested that routine surveillance for hypomagnesemia is done in patients of type 2 diabetes mellitus and studies have shown that treatment of hypomagnesemia with magnesium supplementation can reduce the occurrence of microvascular complications.

REFERENCES:
1. Wahid A, Verma GC, Meena CP, Pathan AR. Study of serum magnesium level in patients with type 2 diabetes mellitus and it's correlation with glycosylated hemoglobin and diabetic complications. Int J Adv Med. 2017 Apr;4(2):311-316.
2. Saproo N, Singh R. Study of serum magnesium levels in diabetes mellitus and its correlation with complications (retinopathy and HbA1c) a cross-sectional study of one year. International Journal of Advances in Medicine Saproo N et al. Int J Adv Med. 2017 Feb;4(1):263-269.
3. Schlinger JL, Grunenberger F, Maier EA, Simon C, Chabrier G, Leroy MJF. Disturbances of plasma trace elements in diabetes - relations with glycemic control. Presse Med. 1988;17:10769.
4. McNair P, Christiansen C, Madsbad S, Lauritzen E, Faber O, Binder C, et al. Hypomagnesemia - a risk factor in diabetic retinopathy. Diabetes. 1978;27:1075-7.
5. Baig MSA, Shamshuddin M, Mahadevappa KL, Attar AH, Shaikh AK. Serum magnesium as a marker of diabetic complications. J Evol Med Dental Sci. 2012;1(3):119-23.
6. Prabhu R and Kunche S. Study of Serum Magnesium and HbA1c in Type 2 Diabetes Mellitus Patients. International Journal of Science and Research. 2015;4(6):2521-24.
7. Vidya B, Prasad K, Rao US, Rao C, Kumari SStudy of Serum Magnesium Levels in Type 2 Diabetes Mellitus at Tertiary Medical Centre, Karnataka, India. Annals of Pathology and Laboratory Medicine. 2016;3(4):284-88.
8. Supriya, Mohanty S, Pinnelli VB, Murgod R, Raghavendra DS. Evaluation of serum copper, magnesium and glycated haemoglobin in Type 2 Diabetes mellitus. Asian J Pharm Clin Res 2013; 6(2):188-90.
9. Dasgupta A, Sarma D, Saikia UK. Hypomagnesemia in type 2 diabetes mellitus. Indian J Endocr Metab 2012;16:1000-3.
10. Kamat S, Morkar D, Madnani S. Serum Magnesium Levels in Type 2 Diabetes Mellitus and its Association with the Microvascular Complications. JMSCR. 2017 ;5(2):18083-89.
11. Suarez A. Decreased insulin sensitivity in skeletal muscle of hypomagnesaemia rats. Diabetologia. 1993;36:82.
12. Rodr guez-Moran M, Guerrero-Romero F. Oral magnesium supplementation improves insulin sensitivity and metabolic control in type 2 diabetic subjects. Diabetes Care 2003;26(4):1147–52.
13. Sajjan NB, Choudhari AS, Desai GM, Dharapur MS, Wali VV. Evaluation of association of serum magnesium with dyslipidaemia in diabetic nephropathy – a case control study. National Journal Of Medical Research. 2014;4(6):318-21.

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14. Grafton G, Baxter MA. The role of magnesium in diabetes mellitus. J Diabetes Complications. 1992;6:143-9.
15. Kahn R, Weir G, King GL, Moses HC, Smith RJ, Jacobson AM. Joslin's diabetes mellitus. 14th ed., New Delhi: Lippincot Williams & Wilkins; 2004.
16. Swain RP, Subudhi BB, MahapatraAK, Bolapreddi V. Bridging Between Disease, Prevalence and Treatment of Diabetes Mellitus: A Review. Int J Pharm Tech Res 2015;7(2):212-28.
17. Mohan V, Sandeep S, Deepa R, Shah B, Varghese C. Epidemiology of type 2 diabetes: Indian scenario. Indian J Med Res 2007;125:217-30.
18. Fujii, S, Takemura, T, Wada, M, Akai T and Okuda K. Magnesium levels in plasma, erythrocytes and urine in patients with diabetes mellitus. Horm. Metab. Res. 1982; 14:161-162.