



STUDY OF SERUM MAGNESIUM LEVEL IN TYPE 2 DIABETES MELLITUS PATIENTS WITH SPECIAL EMPHASIS ON MICROVASCULAR AND MACROVASCULAR COMPLICATIONS

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ABSTRACT

INTRODUCTION: Diabetes is a chronic illness that can affect nearly every organ of body requires continuing medical care and ongoing patient self-management education and support to prevent acute complications and that will reduce the risk of long-term complications. Magnesium deficiency has recently been proposed as a novel factor implicated in the pathogenesis of diabetic complications. Recognising the signs of diabetes associated magnesium deficiency is important because the deficiency can occur long before it is reflected by serum values.

OBJECTIVE: To study the serum magnesium level and establish correlation between hypomagnesemia and micro and macrovascular complications.

MATERIALS AND METHODS: This cross sectional analytical study was carried out in our institution for duration of 1 year. Total of 500 subjects were enrolled in the study. Detailed clinical and laboratory investigations did for diagnosis of complications. The data was analysed using SPSS Version 16.

RESULT: Prevalence of hypomagnesemia in type 2 diabetes was 33% with serum magnesium level 1.31 ± 0.087 mg/dl. Hypomagnesemia has significant association with microvascular complications like retinopathy (66%), nephropathy (67.54%) and neuropathy (54.5%) with p values 0.0001, 0.0005, 0.0001 respectively.

CONCLUSION: Our study showed significant correlation between hypomagnesemia and microvascular complications of type 2 diabetes mellitus. Provided data from this study will help in management and delaying occurrence of complications, also draw attention of clinicians towards a different approach for complications.

KEYWORDS : Type 2 Dm, s. magnesium Level, Complications.

INTRODUCTION -

Diabetes is one of the main threats to human health in the 21st century. Several national and international studies confirmed that diabetes is one of the most common non-communicable disease globally, and is the fourth or fifth leading cause of death in most developed countries because of its adverse effects on vital organs or even on every system of body. It can cause blindness, diplopia, macular edema, lead to end stage renal disease, lower-extremity amputations and increase the risk for stroke, Ischemic heart disease, peripheral vascular diseases, and neuropathy.¹ Microvascular complications such as diabetic retinopathy, diabetic nephropathy are associated with considerable medical and economic impact among person with diabetes. In the UK prospective diabetes study (UKPDS), 37% of patients of newly diagnosed type 2 diabetes developed at least one microvascular complication over a 10 year period.² End stage renal disease develops in 50% of type 1 diabetics with overt nephropathy within 10 years and in >75% by 20 years without specific interventions, 20 to 40% of type 2 diabetics with micro-albuminuria progress to overt nephropathy, but 20 years after onset of overt nephropathy, only about 20% will have progressed to ESRD³. Albuminuria is a marker of greatly increased cardiovascular morbidity and mortality for diabetic patients⁴. It was found that diabetics are 25 times more likely to become legally blind than non diabetics¹. Diabetic retinopathy is characterised by micro-aneurysms, blot hemorrhages and cotton wool spots, and based on this is classified into non-proliferative and proliferative. Neuropathy is the commonest symptomatic complication of diabetes. It can be seen in 15-40% of the diabetic population from various studies. Coronary artery disease is 3 times more common in diabetics, the usual manifestations include angina, acute myocardial infarction, post MI failure, dysrhythmias, complications like shock, conduction disturbances, cardiac failure etc. Magnesium is involved at multiple levels insulin secretion, binding and activity³. It is also involved in many phosphorylation reactions and is a cofactor for ATPase and adenylate cyclase enzymes. Magnesium deficiency has recently been proposed as a novel factor implicated in the pathogenesis of diabetic complications⁴. There is also data to suggest the association between hypomagnesemia and other diabetic co-morbidities like dyslipidemia and hypertension. Some study also showing improvement after supplementation^{5,6}.

MATERIALS AND METHODS:

This cross sectional analytical study was carried out in our institution for duration of 1 year. Total of 500 subjects were enrolled in the study. Informed Patient Consent was obtained before clinical examination. Thorough history taking and clinical examination were done. Patient's proforma was maintained which included all demographic particulars, past medical, surgical, drug, personal and family history. Plasma glucose estimation (FBS and PPBS) was carried out by the glucose oxidase method in the auto analyser. Serum magnesium was estimated by xylydyl blue, colorimetric method. Patients were thoroughly examined and investigated for microvascular and macrovascular complications, patients with Mg level <1.5 mg/dl considered as hypomagnesemic. The patients were grouped as hypomagnesemia of diabetic patients and normomagnesemia of diabetic patients based on their serum magnesium level. Overt nephropathy/macroproteinuria would diagnosed if urinary albumin >300 microg/mg of creatinine or 24 hour urine protein was more than 500mg/24 hours, or if there was evidence of renal failure as evidenced by raised serum creatinine. Retinopathy Present or absent as confirmed by an Ophthalmologist and the diagnosis was made in the presence of micro aneurysms, dot and blot hemorrhages and evidence of macular edema, or any patient who treated by LASER/intervention for retinal detachment/vitreous hemorrhage.

Cardiovascular disease can diagnosed by ECG and echocardiography, or Past history of acute coronary syndrome or Stable angina, History of PTCA/CABG, TMT positivity. Cerebrovascular disease confirmed History of transient ischemic attack/ stroke or CT scan and MRI finding.

INCLUSION CRITERIA:

- All Type 2 Diabetes Mellitus patients

EXCLUSION CRITERIA:

- Patients suffering from Type 1 diabetes
- Alcoholism
- chronic diarrhoea
- Malabsorption syndrome

- Patients on diuretics
- nephrotoxic drugs
- Patients with renal failure
- Patients suffering from thyroid-related disorders

STATISTICAL ANALYSIS:

Statistical evaluation was performed by statistical package for social sciences (SPSS) version 16 for windows statistics program using the Unpaired t test/single factor ANOVA and categorical variables were analysed with chi-squared test and Fisher Exact Test. Correlations of microvascular complications with hypomagnesemia were obtained using Pearson's formula. Arithmetic mean and standard deviation was calculated from our data. A P value <0.05 was considered statistically significant.

OBSERVATION AND RESULTS:

Among the 500 diabetic patients enrolled in the study, we divided them in two groups on the bases of serum magnesium level hypomagnesemic group (Mg level <1.5 mg/dl) and normomagnesemic group (Mg level >1.5 mg/dl). Mean value of serum magnesium level in hypomagnesemic group was 1.31 ± 0.087 mg/dl and 2.61 ± 0.26 mg/dl in normomagnesemic group. Prevalence of hypomagnesemia in type 2 diabetes was 33%, as shown in table no.1 in our study 290 (58%) were male patients and 210 (42%) were females, Mean duration of diabetes in patients was 7.26 ± 2.13 years. Mean BMI in Hypomagnesemic group was 25.79 ± 0.96 and normomagnesemic group was 25.38 ± 0.88. We divided patients on the basis of age in two groups 35-55 Yrs with Mean age 49 ± 4.52 and 55-75 yrs with Mean age 61 ± 4.52.

Prevalence of complications were more common in poor glycemic control as compare to good glycemic control, table no.2 showing highly significant relation between poor glycemic control and complications, prevalence of retinopathy was 51.33% in poor glycemic control and 10.5% in good glycemic control, (p value = 0.001), same as nephropathy and neuropathy also significantly associated with poor glycemic control with p value 0.001 and 0.005 respectively. In macrovascular complications IHD and CVA also significantly associated with poor glycemic control with p value 0.002 and 0.001 respectively.

Hypomagnesemia was significantly associated with microvascular complications. In 500 diabetic patients 175 diagnosed with retinopathy in which 117 (66.85%) patients were hypomagnesemic and 58 (33.28%) patients were normomagnesemic that was statistically significant (p value - 0.0001), 151 patients diagnosed with Nephropathy in which 102 (67.54%) patients were hypomagnesemic and 49 (32.46%) patients were normomagnesemic that was statistically significant (p value - 0.0005), 110 patients diagnosed with Neuropathy in which 60 (54.5%) patients were hypomagnesemic and 50 (45.5%) patients were normomagnesemic that was statistically significant (p value - 0.0001). In macrovascular complications, 130 diagnosed with Ischemic heart disease in which 42 (32.30%) patients were

hypomagnesemic and 88 (67.7%) patients were normomagnesemic that was statistically insignificant (p value - 0.84) and 102 diagnosed with cerebrovascular disease in which 40 (39.21%) patients were hypomagnesemic and 62 (60.79%) patients were normomagnesemic that was statistically insignificant (p value - 0.134). Dyslipidemia also have insignificant relation with hypomagnesemia.

TABLE NO.1 DIFFERENT CHARACTERISTIC OF CASES

CHARACTERISTIC	NUMBER	%
Number of subjects	500	
Hypomagnesemia	165	33%
Normomagnesemia	335	67%
Males	290	58%
Females	210	42%
35-55 Yrs (Mean age 49±4.52)	227	
55-75 yrs (Mean age 61±4.52)	273	
BMI in hypomagnesemic patients	25.79±0.96	
BMI in normomagnesemic patients	25.38±0.88	
Mean duration of DM	7.26 ± 2.13	
FBS	< 126 (113±7.41) 200	40%
	> 126(152±18.60) 300	60%
Retinopathy	175	35%
Nephropathy	151	30.2%
Neuropathy	110	22%
Ischemic heart disease	130	26%
Cerebrovascular disease	102	20.4%
Dyslipidemia	262	54.4%

TABLE NO.2 PREVALENCE OF COMPLICATIONS IN GOOD GLYCEMIC CONTROL AND POOR GLYCEMIC

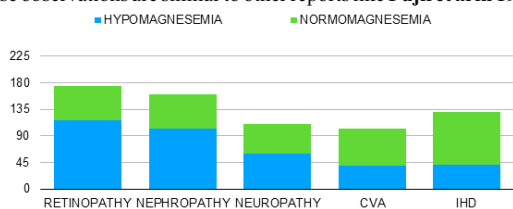
COMPLICATIONS	POOR GLYCEMIC CONTROL (n = 300)	GOOD GLYCEMIC CONTROL (n = 200)	P VALUE
Retinopathy (+/-)	154/146	21/179	0.001
Nephropathy (+/-)	128/160	23/177	0.001
Neuropathy (+/-)	90/210	20/180	0.005
Ischemic heart disease (+/-)	105/195	25/175	0.002
Cerebrovascular disease (+/-)	88/212	14/186	0.001
Dyslipidemia (+/-)	140/160	122/78	0.06

TABLE NO.3 CORRELATION OF HYPOMAGNESEMIA AND COMPLICATIONS

COMPLICATIONS	HYPOMAGNESEMIA	NORMOMAGNESEMIA	P VALUE
Retinopathy	117 (66.85%)	58 (33.28%)	0.0001
Nephropathy	102 (67.54%)	49 (32.46%)	0.0005
Neuropathy	60 (54.5%)	50 (45.5%)	0.0001
Ischemic heart disease	42 (32.3%)	88 (67.7%)	0.84
Cerebrovascular disease	40 (39.21%)	62 (60.79%)	0.134
Dyslipidemia	91 (34.73%)	171 (65.27%)	0.476

DISCUSSION:

In our study, we have observed correlation of hypomagnesemia with micro and macrovascular complications, out of 500 patients 175 were diagnosed with diabetic retinopathy in which hypomagnesemia present in 117 (66.85%) patients, there was a significant difference in prevalence of retinopathy in diabetics with hypomagnesemia and without hypomagnesemia (66.85% vs 33.28%; P value = 0.0001). These observations are similar to other reports like Fujii et al in 1982⁷



was established a close relationship between impaired magnesium balance and retinopathy, who found a marked depletion in plasma and erythrocyte magnesium levels in diabetic patients with advanced retinopathy. Another study Dasgupta et al (2012)⁸ also proved strong relation between hypomagnesemia and retinopathy (64% vs 45.8%). The mechanism by which hypomagnesemia predisposes to diabetic retinopathy is not clear.

Diabetic nephropathy has found in 151 cases among which 102 (67.54%) were having hypomagnesemia. So prevalence of nephropathy was (67.5% v/s 32.46%) in hypomagnesemic and normomagnesemic patients respectively (P value = 0.005).

Similarly Corsonello et al (2000)⁹ demonstrated that diabetic patients with microalbuminuria or clinical proteinuria showed a significant decrease in serum ionized magnesium compared with normal

biuminuria group **Prabhu G et al in 2012**¹⁰ observed higher prevalence of retinopathy (53.84%) in hypomagnesemic cases as compare to normomagnesimic cases, that supports result of our study.

110 Patients were diagnosed with Neuropathy among which 60 (54.5%) were having hypomagnesemic, so prevalence of neuropathy was (54.6% v/s 45.5%) in hypomagnesemic and normomagnesemic groups respectively (P value = 0.0001).

D Leeuw I et al (2004)¹¹ found that intracellular magnesium levels were lower in patients with diabetic peripheral neuropathy **Maria De Lourdes et al in 1998**¹² conducted a studying 128 patients, In which 29 patients with peripheral neuropathy, intracellular Mg levels were lower than in those without it (1.2 ± 0.15 vs. 1.5 ± 0.6 $\mu\text{g}/\text{mg}$ total protein; $P = 0.05$) and improvement in the nerve conduction following supplementation.

In our study, out of 130 patients were diagnosed of ischemic heart disease, only 42 (32.30%) patients having hypomagnesemia, so prevalence of IHD was (32.3%v/s67.7%) in Hypomagnesemic and normomagnesemic patients respectively that indicate non significant relation between hypomagnesemia and IHD in diabetic patients (P value=0.84).

Similarly **Chiristhudas A et al (2016)**¹³ conducted study, in which 8 patients diagnosed IHD, with prevalence of hypomagnesemia was 3 (37.5%) and 5(62.5%) with normomagnesimic, that was statically non significant.

In our study no difference in prevalence of hypomagnesemia was found

in cerebrovascular disease in type 2 DM patients, out of 102 patients of CVA ,40 (39.2%) having hypomagnesemia and 62 (60.79%) patients having normomagnesemia, that was statically non significant (P value = 0.134)

Prabhu G et al (2012)¹⁰ also found similar result, out of the 7 CVA patients 3 (42.85%) patients were hypomagnisemic and 4 (47.15%) patients were normomagnisemic.

In 500 diabetic patients 262 diagnosed with dyslipidemia in which 91(34.78%) patient were hypomagnesemic and 171 (65.22%) patient were normomagnesemic that was statically insignificant (p value - 0.446).

Guerrero –Romero F et al (2006)¹⁴ suggested that hypomagnesemia by a etiopathogenic pathway independent of glycemic status may be involved in the reduction of HDL –cholesterol. **Arpaci D et al (2015)**¹⁵ did not find any assosiation between serum Mg and age, BMI, LDL-C, TG or HDL-C.

CONCLUSION:

The present study concluded that hypomagnesemia is common in type 2 diabetics and magnesium deficiency is associated with diabetic retinopathy, nephropathy, and neuropathy. there is nonsignificant association with macrovascular complications like IHD and CVA, So it may be prudent to consider Magnesium Deficiency as a contributing factor in many Diabetic Complications and in the *Exacerbation* of the disease itself.

LIMITATIONS:

The major limitation of the study was that it was conducted in small population that may not represent the entire population. The study was conducted from those population attending the hospital and thus may reflect high prevalence of complications observed in this study.

The follow up of the cases was not possible to determine the prognostic significance of our findings. Moreover, it could have been possible to correlate and check the reversibility of complications with correction of hypomagnesemia.

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