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THE CORRELATION BETWEEN SERUM MAGNESIUM AND MACROVASCULAR COMPLICATIONS OF TYPE 2 DIABETES MELLITUS

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ABSTRACT:

Background:

Diabetes mellitus and its complications are important cause for morbidity and mortality throughout the World. The aim of this study is to find the correlation between serum magnesium and macrovascular complications of type 2 diabetes mellitus.

Materials and methods:

This is a cross sectional observational study which was conducted in St Martha's Hospital, Department of General Medicine, Bangalore, Karnataka between August 1st 2018 to May 31st 2020with 192 patients. Type 2 diabetic patients with macrovascular complications and Type 2 diabetic patients without macrovascular complications were included in this study.The collected data was analyses by using SPSS software

Results:

Among 192 subjects, 31 (16.1) had CAD, 164(85.4) had PVD, 5(2.6%) had CVA. Of which 8(25.8%), 81(49.4%), 3(60.0%) had hypomagnesemia respectively with P value < 0.05 which was statistically significant.

Conclusion:

We concluded that that serum Mg level was significantly lower in diabetic patients and was strongly associated with all macrovascular complications. The prediction of the onset of complications at an early stage helps in improving mortality and morbidity and to prevent the end organ damage.

Key words: Diabetes mellitus, Macrovascular complications, Hypomagnesemia**.**

INTRODUCTION:

Type 2 diabetes mellitus is an increasing health problem both nationally and throughout the world.Diabetes mellitus (DM) is a complex group of metabolic disorders characterized by chronic increase blood glucose levels(hyperglycemia) which results in altered carbohydrate, protein and fat metabolism due to defects in insulin secretion or insulin action or both(1). The diabetes causes both microvascular and macrovascular complications. Numerous minerals and vitamins produce a role in regulating the insulin secretion and action.

Magnesium (Mg) is the key mineral that plays an important role in regulating the cellular process and is essential for wide range of metabolic reaction. The high levels of magnesium are seen in green leaves, nuts and whole grains (2). Mg is playing an essential role in glucose metabolism and insulin metabolism through various mechanisms (3,4). The normal level of intracellular magnesium helps in regulating insulin secretion but the hypomagnesemia cause insulin resistance (5). When the obese patients with insulin resistance are treated with magnesium supplements in a recent study showed an improvement in both fasting glucose level and insulin sensitivity (6). In a study noted that the lower magnesium level causing twice the chance of occurring type 2 diabetes than with higher level of magnesium(7).Low levels of magnesium have also been attributed to the development and progression of micro and macrovascular complications in Type 2DM.

Hypomagnesaemia is considered as a common electrolyte disease mainly noted in diabetic patients (8). The recent meta- analysis, showed that the supplementation of Mg will results in the improvement of inflammatory marker namely C-reactive protein(9). There are only limited data available in regarding to the association between serum magnesium and type 2 diabetes. Hence in this study we correlate the serum magnesium and macrovascular complications of type 2 diabetes.

MATERIALS AND METHODS:

This study was designed as a cross-sectional observational study, conducted in the Department of General Medicine at St. Martha's Hospital, Bangalore, Karnataka. The study period spanned from August 1, 2018, to May 31, 2020. A total of 192 patients were included in the study, divided into two groups: Type 2 diabetic patients with macrovascular complications and Type 2 diabetic patients without macrovascular complications.

Inclusion and Exclusion Criteria:

- **Inclusion Criteria:** Type 2 diabetic patients with and without macrovascular complications.
- **Exclusion Criteria:** Patients with conditions other than diabetes mellitus that could influence serum magnesium levels were excluded. These conditions included:
    - Nutritional deficiency states
    - Chronic renal or liver failure
    - Hypertension treated with thiazide diuretics
    - Malabsorption syndromes
    - Patients taking magnesium supplements or magnesium-containing antacids
    - Chronic diarrhea
    - Alcohol use

Sample Collection and Measurement: Blood and urine samples were collected from all participants for relevant investigations. Serum magnesium levels were measured using the Dimension® clinical chemistry in-vitro diagnostic assay. This method is a colorimetric endpoint

assay utilizing xylidyl blue to quantitatively determine serum magnesium levels. The measurements were conducted as part of routine laboratory investigations in our facility.

Statistical analysis: The collected data was analyses by using SPSS software. Descriptive statistics such as mean and standard deviation (SD) for continuous variables, frequencies and percentages for categorical variables were determined. Association between variables was analyzed by using Chi-Square test for categorical variables. Level of significance was set at 0.05.

RESULTS:

Table 1: Association between serum magnesium and age group (N=192)

Age (Years)	No.	Hypomagnesemia N (%)
≤40	8	7(87.5)
41-50	36	13(36.1)
51-60	45	21(46.7)
61-70	50	18(36.0)
71-80	41	18(43.9)
>80	12	4(33.3)
Chi-Square Test, P value=0.114, NotSignificant		

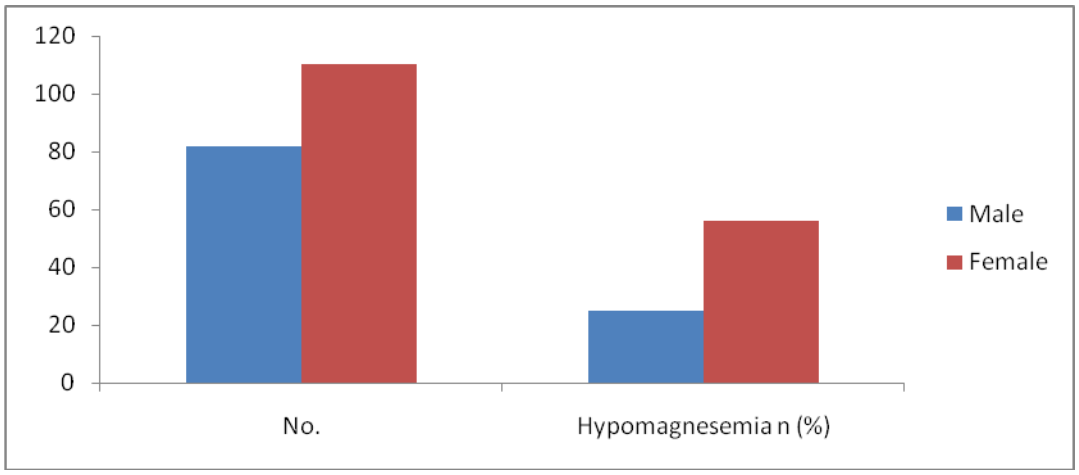

Fig no:1 Association between serum magnesium and gender

The table illustrates the distribution of hypomagnesemia among different age groups in the study population. The age categories are divided into six groups: ≤40 years, 41-50 years, 51-60 years, 61-70 years, 71-80 years, and >80 years. Among patients aged ≤40 years, 87.5% (7 out of 8) had hypomagnesemia. In the 41-50 years age group, 36.1% (13 out of 36) were affected. For those aged 51-60 years, 46.7% (21 out of 45) had hypomagnesemia. The 61-70 years age group had a 36.0% (18 out of 50) prevalence, while the 71-80 years group had 43.9% (18 out of 41) of patients with hypomagnesemia. Lastly, in the >80 years group, 33.3% (4 out of 12) were affected. The Chi-Square test result, with a p-value of 0.114, indicates that the association between age and hypomagnesemia is not statistically significant, suggesting no significant difference in the prevalence of hypomagnesemia across the different age groups in this study.

Table2: Association between Serum Magnesium and Presenting Complaints (N=192)

Presenting Complaints	**No**	**Hypomagnesemian(%)**	**P Value**
CVA			
Headache	3	0	0.136
		81(42.9)	
Sudden Onset Weakness	7	3(42.9)	0.971
		78(42.2)	
Deviation of angle of mouth	4	1(25.0)	0.482
		80(42.6)	
CAD			
Chest Pain	29	6(20.7)	0.011*
		75(46.0)	
Palpitations	8	2(25.0)	0.315
		79(42.9)	
PVD			
Leg Pain	51	24(47.1)	0.411
		57(40.4)	
Skin Discoloration	72	35(48.6)	0.163
		46(38.3)	

The table 2 shows the prevalence of hypomagnesemia among patients with various presenting complaints. For cerebrovascular accident (CVA), none of the 3 patients with headaches had hypomagnesemia, while 42.9% of those with sudden onset weakness (p=0.971) and 25.0% with deviation of the angle of the mouth (p=0.482) were affected, indicating no significant associations. In coronary artery disease (CAD) patients, 20.7% of those with chest pain had hypomagnesemia, which was statistically significant (p=0.011), while 25.0% with palpitations (p=0.315) showed no significant association. Among peripheral vascular disease (PVD) patients, 47.1% with leg pain (p=0.411) and 48.6% with skin discoloration (p=0.163) had hypomagnesemia, both showing no significant associations.

Table 3: Association between Serum Magnesium and CAD based on 2D Echo findings (N=192)

CAD Status	**Hypomagnesemia Present (%)**	**Hypomagnesemia Absent (%)**
Present	8 (9.9%)	23 (20.7%)
Absent	73 (90.1%)	88 (79.3%)

The Chi-Square test yielded a p-value of 0.044, indicating a significant association between CAD and hypomagnesemia. Specifically, 9.9% of patients with CAD had hypomagnesemia compared to 20.7% without hypomagnesemia, while 90.1% of patients without CAD had hypomagnesemia compared to 79.3% without hypomagnesemia. This suggests that hypomagnesemia is significantly associated with the presence of CAD in this study population.

Table 4: Association between Serum Magnesium and PVD based on Doppler

PVD Status	Hypomagnesemia Present (%)	Hypomagnesemia Absent (%)
Present	81 (49.4%)	83 (50.6%)
Absent	0 (0.0%)	28 (100.0%)

The Chi-Square test yielded a p-value of less than 0.001, indicating a highly significant association between PVD and hypomagnesemia. Specifically, 49.4% of patients with PVD had hypomagnesemia, whereas none of the patients without PVD had hypomagnesemia. This significant p-value suggests that hypomagnesemia is strongly associated with the presence of PVD in this study population.

Table5:Association between hypomagnesemia and CVA based on Neuro imaging

CVA Status	Hypomagnesemia Present (%)	Hypomagnesemia Absent (%)
Present	3 (60.0%)	2 (40.0%)
Absent	78 (41.7%)	109 (58.3%)

The Chi-Square test yielded a p-value of 0.413, indicating that the association between CVA and hypomagnesemia is not statistically significant. Specifically, 60.0% of patients with CVA had hypomagnesemia compared to 41.7% of patients without CVA. The lack of significance suggests that there is no strong association between CVA and hypomagnesemia in this study population.

Table 6: Associationbetween HbA1c and Macro-Vascular Complications

Complications	HbA1c < 6.5 (n=28)	HbA1c > 6.5 (n=164)	P-Value
Macrovascular Complications			
CAD	7 (25.0%)	24 (14.6%)	0.168
CVA	0 (0.0%)	5 (3.0%)	0.349
PVD	10 (35.7%)	56 (34.1%)	0.872

The data indicates **CAD:** 25.0% of patients with HbA1c < 6.5 had CAD compared to 14.6% of patients with HbA1c > 6.5. The p-value of 0.168 suggests that this difference is not statistically significant. **CVA:** No patients with HbA1c < 6.5 had CVA, while 3.0% of patients with HbA1c > 6.5 did. The p-value of 0.349 indicates no significant association. **PVD:** 35.7% of patients with HbA1c < 6.5 had PVD compared to 34.1% of those with HbA1c > 6.5. The p-value of 0.872 shows no significant difference between the groups.

DISCUSSION:

Diabetes mellitus, a metabolic disorder is commonly associated with the serum magnesium deficiency. Developing countries like India, the diabetes mellitus is creating a socioeconomic burden. Early age of onset, associated comorbidity, costly drugs, and investigations are made this disease more challenging for primary care health professionals.

In this study, we found that serum Mg level was significantly lower in diabetic patients and is strongly associated with macrovascular complications. Among 192 subjects, 31 (16.1) had CAD, 164(85.4) had PVD, 5(2.6%) had CVA. Of which 8(25.8%), 81(49.4%), 3(60.0%) had hypomagnesemia respectively with Pvalue=0.002, 0.04, 0.001 in CAD, PVD which was statistically significant.

In our study, HbA1c value was not statistically significant with the low serum magnesium level though hypomagnesemia was correlating with majority of macrovascular complications (except cerebrovascular disease). The possible explanation for the same is that we have taken a single value of HbA1c and not the serial values.

Baig et al (10),found similar results and suggested that hypomagnesemia may act through inhibition of prostacyclin receptor function producing an imbalance between prostacyclin and thromboxane effect which has marked atherogenic potential responsible for microvascular complications.

Studies by Lecube et al (11) and Dasgupta et al (12) on diabetes and hypomagnesemia found significant negative correlation between serum magnesium and fasting plasma glucose. Intracellular serum magnesium plays a key role in regulating insulin action, insulin- mediated glucose uptake, and vascular tone. Reduced intracellular Mg concentration result in a defective tyrosine-kinase activity, post receptor impairment in insulin action, and worsening of insulin resistance in diabetic patients.

Aradhana Sharma et al (13) also found that serum magnesium levels were significantly lowered in patients with diabetic complications when compared to diabetic patients without complications. In our study we found that the lower magnesium level causes macrovascular complications.

CONCULSION:

We concluded that that serum Mg level was significantly lower in diabetic patients and was strongly associated with all macrovascular complicationsHence serum magnesium level have negative correlation with macrovascular complications in patients with type 2 diabetes mellitus.So, that we can predict the onset of complications at an early stage and hence mortality and morbidity can be improved by preventing the end organ damage.

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