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A STUDY OF SERUM MAGNESIUM IN TYPE 2 DIABETES MELLITUS AND ITS CORRELATION WITH GLYCEMIC CONTROL AND DIABETIC MICROVASCULAR CHANGES

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ABSTRACT

Background- According to the International Diabetes Federation's (IDF) Sixth Diabetes Atlas, there were more than twice as many instances of diabetes in India in 2013 as there were in 2000, with an estimated 65.1 million cases. The fact that Indians have T2DM at an earlier age than western cultures is quite concerning. Diabetes also develops in along with the little weight increase. Patients with diabetes frequently lack magnesium; 25–39% of diabetics have low blood magnesium levels. There is limited research on estimation magnesium levels in diabetic individuals with poor glycaemic control, and its impact on microvascular complications. Hence, we performed this study to correlated the serum magnesium levels with HbA1c and the microvascular complications associated with type II diabetes mellitus.

Methods- This was a case-control study conducted in the department of General medicine in a tertiary care hospital conducted between January 2022 and June 2023. The study included all patients with Type 2 Diabetes mellitus patients on basis of ADA 2018 Criteria. Non-Critically ill, age >35 years and those consenting for the study.

Results- Majority of the study population belonged to 56-65 years (32.0%). There was a significant negative correlation of Serum Magnesium (mg/dl) with RBS (mg/dl), FBS (mg/dl), PPBS (mg/dl) and HbA1c % with Pearson correlation being -0.513, -0.503, -0.595 and -0.607 respectively. When we correlated the magnesium levels with retinopathy and nephropathy, we observed that there was a significant correlation. (P value < 0.05).

Conclusion- We have observed with this study that there is a significant negative correlation between serum magnesium levels and fasting, postprandial, and HbA1c % blood glucose levels. Patients with low serum magnesium have more severe diabetic retinopathy changes.

Keywords- diabetic retinopathy, hypomagnesaemia, glycaemic control

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INTRODUCTION

According to the International Diabetes Federation's (IDF) Sixth Diabetes Atlas, there were more than twice as many instances of diabetes in India in 2013 as there were in 2000, with an estimated 65.1 million cases.[1,2] It was estimated that by 2030, Diabetes may impact up to 79.4 million people in India, while the number of people with the condition in China (42.3 million) and the United States (30.3 million) would also rise significantly. [3,4]However, given that the majority of the population in India is rural, these numbers may not accurately reflect or offer a prevalence. By 2030, it is estimated that up to 79.4 million individuals in India would be affected by Diabetes. [2,3] Globally, the increased prevalence of Type 2 Diabetes mellitus has been shown to have significant economic and morbidity consequences. [5]

Indians have lower thresholds for environmental risk factors and a higher ethnic and genetic sensitivity to the illness.[6] The fact that Indians have T2DM at an earlier age than western cultures is quite concerning. Diabetes also develops in along with the little weight increase. [6]Diet is commonly recognized to have a significant impact in the development of diabetes mellitus (DM) and its accompanying consequences. Diabetes is regarded as a lifestyle illness. Retinopathy, neuropathy, and nephropathy are examples of microvascular problems. Coronary heart disease, peripheral artery disease, and cerebrovascular disease are examples of macrovascular complications.[7]

Inflammation brought on by metabolism has been hypothesized to be a key step in the aetiology of T2DM. It has also been discovered that DM alters the metabolism of a number of minerals, and these compounds may have unique functions in the pathogenesis and progression of this disease. The most important of these elements is magnesium. It is crucial for the metabolism and phosphorylation of glucose. Its lack has been linked to diabetic problems such insulin resistance, carbohydrate intolerance, and dyslipidemia[8].

Due to its ability to increase insulin sensitivity and shield against diabetes and its consequences, magnesium has drawn a lot of interest. Although hypomagnesemia has been connected to additional risk factors for the development of diabetic retinopathy in Caucasian diabetics, black African diabetics have not shown this linkage [8]. Low magnesium levels in T2DM patients have been associated with autonomic dysfunction, altered insulin metabolism, glomerular hyperfiltration, osmotic diuresis, metabolic acidosis, hypophosphatemia, and hypokalemia. Additionally connected to poor glycemic management and the presence of both microvascular and macrovascular problems are low magnesium concentrations. The incidence of incident T2DM was also found to be predicted by plasma magnesium [9].

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Patients with diabetes frequently lack magnesium; 25–39% of diabetics have low blood magnesium levels.[10] In T2DM patients, a lack of magnesium has a detrimental effect on insulin sensitivity and glucose control.[11] Therefore, has an impact on the development of problems such retinal, vascular atherosclerosis, and nephropathy in people with diabetes.[2] Increased magnesium consumption in patients has been linked to lower T2DM risk, according to several major studies.[12] Numerous experimental metabolic research on people have demonstrated that taking more magnesium has positive effects on insulin sensitivity, insulin action, and glucose metabolism.[13]

There is limited research on estimation magnesium levels in diabetic individuals with poor glycaemic control, and it's impact on microvascular complications. Hence, we performed this study to correlated the serum magnesium levels with HbA1c and the microvascular complications associated with type II diabetes mellitus.

MATERIALS AND METHODS\

This was a case-control study conducted in the department of General medicine in a tertiary care hospital conducted between January 2022 and June 2023.. The study included all patients with Type 2 Diabetes mellitus patients on basis of ADA 2018 Criteria. Non-Critically ill, age >35 years and those consenting for the study. The study excluded patients with Type 1 DM, patients in sepsis, CRF, CLD, pregnancy, lactation, malabsorption states and consuming drugs affecting magnesium levels. 50 patients were taken as cases, and 50 non-critical, non-diabetic patients were taken as controls.

Once admitted, all routine investigations were performed, including FBS, PPBS HbA1c, serum magensium and renal functions. In those patients with evidence of nephropathy, they were categorised based on the eGFR.

Fundoscopy examination will be carried out by single observer in ophthalmology department in the institution.Patients were divided into 4 groups, No DR, NPDR, PDR and Macular oedema.

Statistical Analysis

Master chart extracting data from entire study population will be created using their clinical and laboratory records.All the data obtained will be analysed statistically using software like Microsoft Excel, IBM SPSS.Appropriate standard statistical analysis methods will be used to determine factors associated with the outcome.A 'p' value of <0.05 will be considered significant.

RESULTS

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Majority of the study population belonged to 56-65 years (32.0%) followed by 36-45 years(24%) & Above 65 years (24.0%), 46-55 years (16.0%) and 25-35 years (4.0%).There were 60.0% males and 40.0% females

It was observed that majority of the study population had mild NPDR.

Table 1: Distribution of study population according to Fundoscopy findings

Fundoscopy (by Direct Opthalmoscope)	Frequency	Percent
Mild NPDR	25	50.0%
Moderate NPDR	16	32.0%
Severe NPDR	7	14.0%
PDR	2	4.0%

Mean Serum Magnesium (mg/dl) was significantly low among PDR compared to Severe NPDR which was significantly low than moderate NPDR than mild PDR.

Table 2: Correlation between Serum Magnesium and Fundoscopy findings

	Serum Magnesium (mg/dl)				
	Mean	Std. Deviation	F-value	p-value	Post-hoc comparisons
Mild NPDR	2.10	0.21	10.633	0.001*	
Moderate NPDR	1.91	0.23			
Severe NPDR	1.79	0.07			
PDR	1.53	0.16			

There was a significant negative correlation of Serum Magnesium (mg/dl) with RBS (mg/dl), FBS (mg/dl), PPBS (mg/dl) and HbA1c %.

Table 3: Correlation between Serum Magnesium and Blood sugar

		Serum Magnesium (mg/dl)
RBS (mg/dl)	Pearson Correlation	-0.513
	p-value	0.001*
FBS (mg/dl)	Pearson Correlation	-0.503
	p-value	0.001*
PPBS (mg/dl)	Pearson Correlation	-0.595
	p-value	0.001*

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Hypomagnesemia was significantly more among PDR compared to severe NPDR which was significantly more than Moderate NPDR which was significantly more than Mild NPDR.

Table 4: Distribution of study population according to Serum Magnesium

Magnesium levels	Fundoscopy (by direct opthalmoscope)			
	Mild NPDR	Moderate NPDR	Severe NPDR	PDR
Normal (1.7 to 2.2 mg/dL)	24	12	4	0
	96.0%	75.0%	57.1%	0.0%
Hypomagnesemia (< 1.7 mg/dL)	1	4	3	2
	4.0%	25.0%	42.9%	100.0%
χ^2 value = 49.562, p-value = 0.001*				

Mean RBS (mg/dl), FBS (mg/dl), PPBS (mg/dl) and HbA1c % was significantly more among PDR compared to Severe NPDR which was significantly more than moderate NPDR which was significantly more than Mild NPDR.

Magnesium levels	Nephropathy (based on eGFR)			
	No CKD	CKD I-III	CKD IV	CKD V
Normal (1.7 to 2.2 mg/dL)	25	11	5	1
Hypomagnesemia (< 1.7 mg/dL)	2	3	4	1
χ^2 value = 47.221, p-value = 0.001*				

Similarly, when we correlated the magnesium levels with the nephropathy, and we observed a positive correlation.

DISCUSSION

Diabetes mellitus has a higher incidence of hypomagnesemia than other endocrine and metabolic illnesses, ranging from 25 to 39%.The pathophysiology of numerous diabetes complications has recently been linked to magnesium insufficiency as a unique component. Diabetic problems can both be a result of and a cause of hypomagnesemia. Osmotic diuresis decreases renal tubular absorption of Magnesium, insulin sensitivity, which alters intracellular magnesium transport and increases extracellular magnesium loss, and frequent

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use of diuretics are the variables that cause magnesium insufficiency in people with diabetes mellitus.[6,8] In earlier research, a lack of Magnesium has been linked to insulin resistance, carbohydrate intolerance, dyslipidemia, and hypertension.

Majority of the study population belonged to 56-65 years (32.0%). Bhoi and Gohel et al[7] found that the mean age of patients in Group I, Group II, and Group III are 54±5, 57±6, and 58±5 years, respectively.

In the current study, there were 60.0% males and 40.0% females. Bhoi and Gohel et al[7] found that among Group II, 26 were males and 24 were females; among Group III, 30 were males and 20 females; among Group I and 27 were males and 23 females.

There was a significant negative correlation of Serum Magnesium (mg/dl) with RBS (mg/dl), FBS (mg/dl), PPBS (mg/dl) and HbA1c % with Pearson correlation being -0.513, -0.503, -0.595 and -0.607 respectively. Similar to our findings, Ganiger et al.[6] showed a significantly significant inverse relationship between serum magnesium and glycosylated hemoglobin (HbA1c). Misra et al.[9] found a negative link between the mean levels of serum magnesium (2.08±0.4 mg/dL), the mean levels of fasting plasma sugar (159.72±71.60 mg/dL), and the mean levels of postprandial sugar (222.76±100.86 mg/dL).

Bhoi and Gohel. et al [7] reported that Serum magnesium concentration and levels of HbA1c, PPBS, and Fasting Blood Glucose (FBS) all exhibited statistically significant negative correlations. Prabhu et al.[4] discovered that 18 of the 19 patients with hypomagnesemia had HbA1c levels higher than 7%.

These results matched Kundu et al.,[10] who reported that serum magnesium levels were significantly lower in patients with diabetic retinopathy compared with diabetics without retinopathy, and the prevalence of hypomagnesemia was 44%.

In the study of Kundu et al [10] magnesium levels and glycemic control in diabetics were also positively correlated. When the association between magnesium levels and the degree of diabetes management was established, it was found that diabetics with poorly managed diabetes had lower blood and urine magnesium levels, respectively, and higher levels than diabetics with decently controlled diabetes. HbA1c tests roughly correlate with mean plasma glucose readings from the two to three months prior. Higher HbA1c percentages signify subpar glycemic management in the preceding months.

Correlation between Serum Magnesium and Diabetic Retinopathy

In our study, mean Serum Magnesium (mg/dl) was significantly low among the population of PDR compared to severe NPDR, which is significantly lower in moderate PDR followed

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by mild NPDR. Similar to our study, Vijayapriya et al. [15] found that the median magnesium level among those with mild NPDR was 1.90. Those with mild NPDR, severe NPDR, proliferative retinopathy, and no retinopathy were 1.90, 1.75, 1.8, and 2.10, respectively.

The mean serum magnesium levels between cases and controls were 1.67 mg/dl and 2.03 mg/dl, respectively. Prabhu et al [4] discovered that Magnesium levels in serum were, on average, 1.74±0.32mg/dl. 25% of the group had serum magnesium levels less than or equivalent to 1.5 mg/dl. Serum magnesium levels were shown to be lower in patients with diabetes that had been present for an extended period.

Yossef et al. [11] stated that Diabetic patients had significantly lower serum magnesium levels than the control group (P=0.007). In 56 (80%) patients, hypomagnesemia was found, but not in any of the controls. Wahid et al. [13] found that between diabetics and the control group, there was a statistically significant difference in the prevalence of hypomagnesemia (34% versus 6%) and serum magnesium levels. Sathyaseelan and Sundaram[12] stated that between diabetes patients and controls, the mean serum magnesium levels were 1.28±0.48 mg/dl and 2.23±0.21 mg/dl, respectively.

Wahid et al. [13] found that between diabetics and the control group, there was a statistically significant difference in the prevalence of hypomagnesemia (34% versus 6%) and serum magnesium levels. Compared to normomagnesemic diabetics, hypomagnesemia diabetics had significantly higher levels of FBS, PPBS, and HbA1C. Compared to normomagnesemic diabetics, a significant percentage of hypomagnesemia diabetics (47.06% versus 19.70%).

Serum magnesium and diabetic nephropathy

In a study by Zhang et al (14), The research results showed that low concentration of serum magnesium and four common diabetic complications – diabetic retinopathy, diabetic nephropathy, diabetic neuropathy and diabetic macroangiopathy – exists association, but no obvious correlation with other comorbidities like hypertension. This was similar to the findings in our study.

In a study by Sakaguchi et al (8) they observed that in 455 retrospectively recruited patients with diabetic nephropathy, 102 progressed to ESRD during follow-up (median, 23 months). A multivariate Cox proportional hazards model showed that after adjustment for various demographic factors and laboratory data, the Low-Mg group had a 2.12-fold higher risk of ESRD than the High-Mg group (95% CI 1.28–3.51; P = 0.004). In contrast, 135 of the nondiabetic CKD subjects progressed to ESRD during follow-up (median, 44 months). No significant difference in outcome was found between the Low- and High-Mg groups of this population (adjusted hazard ratio, 1.15; 95% CI 0.70–1.90; P = 0.57).

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CONCLUSION

We have observed with this study that there is a significant negative correlation between serum magnesium levels and fasting, postprandial, and HbA1c % blood glucose levels. Patients with low serum magnesium have more severe diabetic retinopathy changes. It is crucial to assess magnesium levels in diabetes mellitus patients because those with poorly managed diabetes had serum magnesium levels that were lower than those with well-controlled diabetes.

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