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Corresponding Author
A. Mohammed Hussain,
Department of General Medicine, Aarupadai Veedu Medical College, Vinakaya Missions Research Institute (VMRF-DU), Puducherry, India

Author Designation
[1]Post-Graduate
[2]Professor
[3]Assistant Professor

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Serum Magnesium Level in Type 2 Diabetes Mellitus Patients with and Without Microvascular Complication and Its Association with Glycemic Control

[1]A. Mohammed Hussain, [2]K. Jayasingh and [3]I. Balaji
[1-3]Department of General Medicine, Aarupadai Veedu Medical College, Vinakaya Missions Research Institute (VMRF-DU), Puducherry, India

ABSTRACT
This study aims to investigate the serum magnesium levels in Type 2 Diabetes Mellitus (T2DM) patients with and without microvascular complications and to explore the association between serum magnesium levels and glycemic control. An observational cross-sectional study was conducted from June 2022-2024 at Aarupadi Veedu Medical College, Puducherry. A total of 120 T2DM patients were included, categorized into good (HbA1c $\leq$7%) and poor glycemic control (HbA1c >7%) groups. Clinical parameters, including serum magnesium, fasting and postprandial blood sugar, HbA1c and microvascular complications, were assessed. Statistical analysis was performed using parametric tests. The study found that patients with poor glycemic control had significantly lower serum magnesium levels (1.70±0.24 mg/dL) compared to those with good control (2.09±0.19 mg/dL, p=0.001). Additionally, lower magnesium levels were strongly associated with the presence of microvascular complications such as retinopathy, nephropathy, and neuropathy. The correlation between serum magnesium and microvascular complications was significant (r=0.840, p=0.0001). Lower serum magnesium levels are associated with poor glycemic control and increased risk of microvascular complications in T2DM patients. Regular monitoring and potential magnesium supplementation could improve outcomes, emphasizing the need for comprehensive management strategies that include micronutrient assessment.

INTRODUCTION

Globally, type 2 diabetes mellitus (T2DM) considered as significant public health problem. Type 2 Diabetes Mellitus (T2DM) is a chronic metabolic disorder characterized by insulin resistance and relative insulin deficiency, leading to hyperglycemia. It is a significant global health concern due to its rising prevalence and the serious complications associated with it. Among these complications, microvascular complications, such as diabetic retinopathy, nephropathy and neuropathy, are particularly concerning as they significantly impact the quality of life and increase the morbidity and mortality rates in diabetic patients. T2DM is characterised by persistently high blood sugar levels, which are caused by a complicated interaction between insulin resistance and decreased insulin production. The International Diabetes Federation estimates that 439 million people worldwide will have diabetes by 2030 as a result of the disease rising prevalence[1].

The long-term consequences of type 2 diabetes are extremely dangerous for both patient safety and healthcare institutions. Microvascular problems are of special concern. These include diabetic retinopathy, nephropathy and neuropathy. These issues can have disastrous results, including blindness, renal failure, and crippling nerve damage, which can drastically lower patient quality of life and raise medical expenses[2].

Magnesium is an essential mineral involved in numerous biochemical processes, including glucose metabolism and insulin action. It plays a critical role in the regulation of glycemic control, as it acts as a cofactor for many enzymes involved in carbohydrate metabolism and the maintenance of insulin sensitivity. Hypomagnesemia, or low serum magnesium levels, is a common finding in patients with T2DM and has been associated with poor glycemic control and increased risk of developing diabetic complications[3]. Magnesium (Mg) is a necessary mineral that is involved in more than 300 metabolic processes in the human body. Interestingly, several of these responses are very closely related to insulin activity and glucose metabolism. A possible correlation between hypomagnesemia, and type 2 diabetes has been highlighted by recent studies. According to studies, people with diabetes may have reduced magnesium levels than those in general. Scientific curiosity over magnesium's potential function in the treatment of diabetes has been aroused by this observation[4,5]. Research into the fascinating connection between magnesium and diabetes is warranted. The prevalence of hypomagnesemia in individuals with type 2 diabetes will be examined in this study. To find out if there is a substantial variation in magnesium levels between patients with and without microvascular problems, we will further stratify this data. We will investigate the relationship between glycemic management and blood magnesium levels in individuals with type 2 diabetes. The main indicator of glycemic control will be haemoglobin A1c (HbA1c), which offers important information about how well individuals are controlling their blood sugar levels[6]. The exact mechanisms linking magnesium levels with diabetes and its complications are not fully understood. However, studies suggest that magnesium deficiency may exacerbate insulin resistance, impair insulin secretion, and increase oxidative stress and inflammation, all of which contribute to the progression of diabetes and its complications. Moreover, microvascular complications in diabetes are associated with alterations in microcirculation and endothelial function, which may be influenced by magnesium levels. Better T2DM management tactics may be greatly aided by an understanding of these linkages. Healthcare practitioners may be able to investigate the possible advantages of magnesium supplementation as a supplemental strategy by recognising potential magnesium deficits, especially in patients with microvascular problems or poor glycemic control. By taking this strategy, diabetes care might be optimised and perhaps the development of catastrophic complications could be delayed or prevented[7]. This study aims to investigate the serum magnesium levels in T2DM patients with and without microvascular complications and to explore the association between serum magnesium levels and glycemic control.

MATERIALS AND METHODS

The observational cross-sectional study conducted from June 2022-2024 at the outpatient and inpatient departments of the Department of General Medicine at Aarupadi Veedu Medical College, a tertiary care center in Puducherry. The ethical committee approval was obtained with ethical approval number (IHEC No. AV/IHEC/2022/080) from the institutional Human Ethics Committee of Aarupadai Veedu Medical College and Hospital in Kirumampakam, Puducherry. The study aimed to include patients over the age of 18 with Type 2 diabetes mellitus, using HbA1c levels to differentiate between good ($\leq$7%) and poor (>7%) glycemic control. Exclusion criteria included patients with known magnesium deficiency and those unwilling to provide informed consent. A total sample size of 120 patients (60 in each group) was calculated based on a similar study conducted by Bharthkumar k *et al.* in the year 2023, assuming a prevalence of hypomagnesemia of 26% in patients with good glycemic control and 56% in those with poor control, with a 5% level of significance and 90% power[8]. Convenience sampling was used for

participant selection. The study procedure involved obtaining informed consent, collecting demographic data and assessing various clinical parameters, including serum magnesium, fasting and postprandial blood sugar levels, HbA1c, serum creatinine, and urine albumin/creatinine ratio. Additionally, participants underwent ophthalmic evaluations to check for diabetic retinopathy and neurological examinations to assess for diabetic neuropathy, along with kidney function assessments to rule out diabetic nephropathy. To analyse the data SPSS (IBM SPSS Statistics for Windows, Version 26.0, Armonk, NY: IBM Corp. Released 2019) and Excel Sheet were used to enter the data. The Normality tests, Kolmogorov-Smirnov and Shapiro-Wilks tests results revealed that the data follows normal distribution. Therefore, to analyse the data, parametric test was applied. Descriptive statistics determined the frequency, percentage, mean and standard deviation for the variables. Independent t test was applied to find the statistical significance between serum magnesium levels. The significance level is fixed as 5% (a=0.05). P-value <0.05 is considered to be statistically significant.

RESULTS AND DISCUSSIONS

The observational cross-sectional study included 120 patients with Type 2 Diabetes Mellitus (T2DM), divided into two groups based on glycemic control: good control (HbA1c ≤7%, n=60) and poor control (HbA1c >7%, n=60). The study was conducted from June 2022 to June 2024 at Aarupadi Veedu Medical College, Puducherry. Table 1 depicts the frequency and percentage distribution of age groups ranged from below 40 to above 60 years. There were 10 patients below 40 years (8.3%). There were 35 patients in the age group of 41-50 years (29.2%). There were 34 patients in the age group of 51-60 years (28.3%). There were 41 patients aged more than 60 years (34.2%) in this present study. Table 2 depicts the gender distribution of Study subjects. The percentage distribution of male and female subjects is 56.7% and 43.3% in this present study. Table 3 depicts the distribution of glycemic control among the study participants. Of the total participants, 57 individuals (47.5%) were classified as having good glycemic control, characterized by an HbA1c level of 7% or less. In contrast, 63 participants (52.5%) were classified as having poor glycemic control, with HbA1c levels exceeding 7%. Table 4 depicts the descriptive statistics (mean, standard deviation, minimum and maximum) for various measurable variables, including age, FBS, PPBS, HbA1c, serum creatinine, serum magnesium and urine albumin among the study participants. Table 5 depicts the mean and standard deviation of serum magnesium levels in relation to glycemic control among the study participants. The mean serum magnesium level for participants with good glycemic control (HbA1c ≤7%) was 2.09±0.19 mg/dL, with a range from 1.60-2.40 mg/dL. For participants with poor glycemic control (HbA1c >7%), the mean serum magnesium level was significantly lower at 1.70±0.24 mg/dL, with a range from 1.30-2.20 mg/dL. P-value of 0.001 indicate that the difference in serum magnesium levels between the two groups is statistically significant. Table 6 depicts the association between microvascular complications and glycemic control among the study participants. The data indicates that among those with good glycemic control (HbA1c ≤7%), only 7 participants (12.3%) had microvascular complications, while 50 participants (87.7%) did not. In contrast, a significantly higher proportion of participants with poor glycemic control (HbA1c >7%) experienced microvascular complications, with 51 participants (81.0%) affected and only 12 participants (19.0%) not experiencing these complications. The P-value of 0.0001 suggests a statistically significant association between poor glycemic control and the presence of microvascular complications. Table 7 depicts the relationship between serum magnesium levels and the presence of microvascular complications among the study participants. The mean serum magnesium level for participants with microvascular complications was 1.63±0.17 mg/dL, with a range from 1.30-1.90 mg/dL. Conversely, participants without microvascular complications had a significantly higher mean serum magnesium level of 2.12±0.16 mg/dL, ranging from 1.70-2.40 mg/dL. The P-value of 0.0001 indicates a statistically significant difference in serum magnesium levels between those with and without microvascular complications. This finding suggests that lower serum magnesium levels are strongly associated with the presence of microvascular complications in patients with Type 2 diabetes mellitus. Table 8 depicts the correlation between serum magnesium levels and microvascular complications. There is a significant positive correlation found (r=0.840, p=0.0001) between serum magnesium levels and microvascular complications. Overall, these results support the hypothesis that low serum magnesium levels are strongly associated with an increased risk of microvascular complications in T2DM patients. This correlation underscores the potential importance of monitoring and managing magnesium levels as part of comprehensive diabetes care to potentially reduce the risk of complications.

Table 1: Age-Wise Group Distribution Among the Study Participants

Age group	Frequency	Percentage
≤40 yrs	10	8.3
41-50 yrs	35	29.2
51-60 yrs	34	28.3
>60 yrs	41	34.2

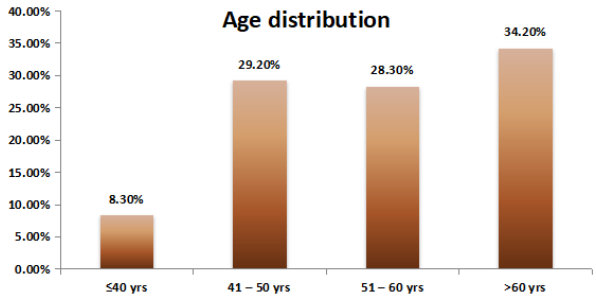

Fig 1: Age Group Distribution of the Study Participants

Table 2: Frequency and Percentage Distribution of Gender Distribution Among the Study Participants

Gender	Frequency	Percentage
Male	68	56.7%
Female	52	43.3%

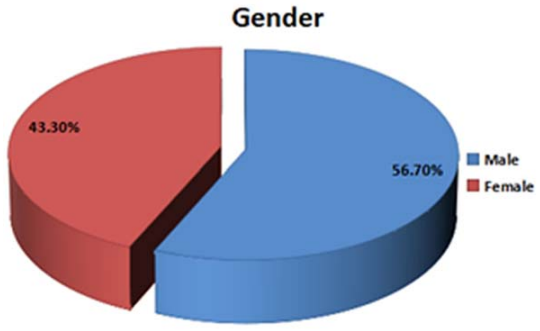

Fig 2: Gender Distribution of the Study Participants

Table 3: Frequency and Percentage Distribution of Glycemic Control Among the Study Participants

Glycemic Control	Frequency	Percentage
Good	57	47.5
Poor	63	52.5

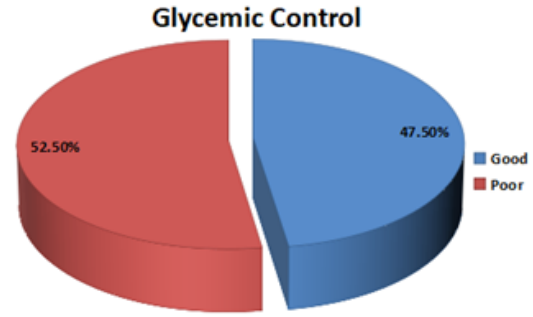

Fig 3: Frequency and Percentage Distribution of Glycemic Control of the Study Participants

Table 4: Descriptive Statistics for Measurable Variables

Variable	Minimum	Maximum	Mean ± SD
Age	34.00	73.00	55.38 ± 10.35
FBS	88.00	158.00	118.71 ± 18.50
PPBS	128.00	210.00	167.66 ± 22.24
HbA1C	5.40	9.10	7.23 ± 1.05
Serum Creatinine	0.70	1.30	0.99 ± 0.14
Serum Magnesium	1.30	2.40	1.88 ± 0.29
Urine Albumin	10.00	50.00	135.73 ± 155.44

Table 5: Mean and Standard Deviation Between Serum Magnesium Mean and Glycemic Control Among the Study Groups

Variable	Glycemic Control	Mean±SD	Min	Max	F value	P-value
Serum Magnesium	Good	2.09 ± 0.19	1.60	2.40	9.801	0.001*
	Poor	1.70 ± 0.24	1.30	2.20		

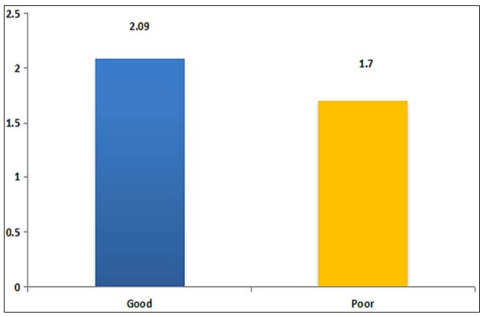

Fig 4: Mean and Standard Deviation Between Serum Magnesium Mean and Glycemic Control of the Study Groups

Table 6: Association Between Microvascular Complications and Glycemic Control Among the Study Participants

	Glycemic Control				
	Good		Poor		
Microvascular Complications	Frequency	Percentage	Frequency	Percentage	P value
Yes	7	12.3	51	81.0	0.0001*
No	50	87.7	12	19.0	

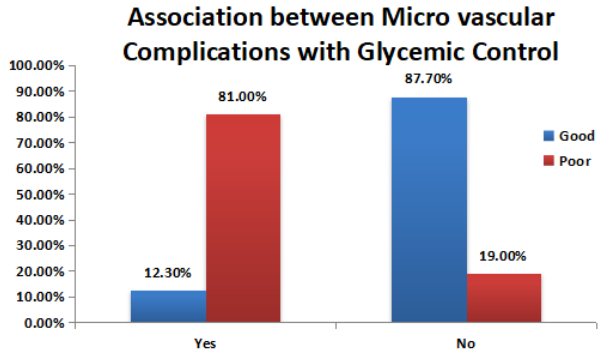

Fig 5: Association Between Microvascular Complications and Glycemic Control of the Study Participants

Table 7: Association Between Serum Magnesium and Microvascular Complications Among the Study Participants

Variable	Micro Vascular Complication	Mean±SD	Min	Max	F value	P value
Serum Magnesium	Yes	1.63 ± 0.17	1.30	1.90	-15.975	0.0001*
	No	2.12 ± 0.16	1.70	2.40		

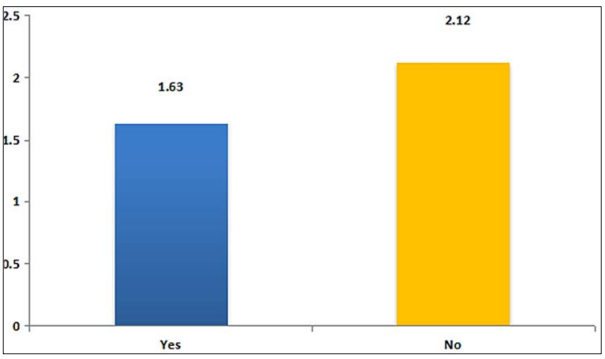

Fig 6: Association Between Serum Magnesium and Microvascular Complications of the Study Participants

Table 8: Correlation Between Serum Magnesium and Microvascular Complications Among the Participants

			Correlations	
			Serum Magnesium	Microvascular Complications
Spearman's rho	Serum Magnesium	Correlation Coefficient	1.000	.840**
		Sig. (2-tailed) p value	.	.000
		N	120	120
	Microvascular Complications	Correlation Coefficient	.840**	1.000
		Sig. (2-tailed)	.000	.
		N	120	120

**. Correlation is significant at the 0.01 level (2-tailed).

(Table 8) depicts the correlation between serum magnesium levels and microvascular complications. There is a significant positive correlation found (r=0.840, p=0.0001) between serum magnesium levels and microvascular complications.

The present study investigated various factors associated with glycemic control and microvascular complications among individuals with Type 2 diabetes mellitus. The findings revealed important insights into the demographic distribution, biochemical markers, and their relationships with diabetes management and complications. The study conducted aims to shed light on the significant differences in serum magnesium levels between Type 2 Diabetes Mellitus (T2DM) patients with and without microvascular complications and to understand its association with glycemic control. The analysis of the data provides compelling evidence that serum magnesium levels are markedly lower in patients with poor glycemic control and those suffering from microvascular complications compared to their counterparts with good glycemic control and without such complications. These findings are in alignment with several key studies and provide a deeper understanding of the underlying mechanisms and implications for clinical practice.

The observed mean serum magnesium level in patients with poor glycemic control was significantly lower (1.70±0.24 mg/dL) than in those with good glycemic control (2.09±0.19 mg/dL), with a p-value of 0.0001. "This disparity is consistent with the results of studies conducted by Barbagallo et al. in the year 2010 and Rodriguez-Moran *et al.* in the year 2003, which found that hypomagnesemia is prevalent among poorly controlled diabetic patients[9,10]. The same study conducted by Barbagallo *et al.* 2010 highlighted that magnesium plays a major role in insulin-mediated glucose uptake, and its deficiency can lead to insulin resistance, thereby exacerbating glycemic control[9]. Similar study conducted by Rodriguez et al. in the year 2003 also demonstrated that low magnesium levels are a common finding in patients with uncontrolled diabetes, reinforcing the notion that maintaining adequate magnesium levels is essential for effective diabetes management[10]. Hypomagnesemia's impact on insulin secretion and action further underscores its role in diabetes. The study conducted by Sales *et al.* in the year 2006 elucidated, magnesium deficiency impairs insulin's ability to act effectively, leading to higher blood glucose levels[11]. Our study corroborates this by showing a clear correlation between lower magnesium levels and elevated HbA1C levels. Given that HbA1C is a key indicator of long-term glycemic control, the significant difference in HbA1C levels between the good control group (6.46±0.72%) and the poor control group (7.92±0.80%) further emphasizes the importance of magnesium in managing diabetes.

Patients with microvascular complications exhibited significantly lower serum magnesium levels (mean 1.785 mg/dL) compared to those without complications (mean 1.978 mg/dL), with a t-statistic of -2.883 and a p-value of 0.0049. This finding is consistent with the study conducted by Pham et al. in the year 2007 and Rude et al. in the year 2006, which report that hypomagnesemia is associated with an increased risk of developing microvascular complications, such as diabetic retinopathy, nephropathy and neuropathy[12,13]. A similar study conducted by Pham et al. in the year 2007 identified a direct relationship between low magnesium levels and the severity of these complications, suggesting that magnesium supplementation could potentially mitigate these risks[12].

Magnesium's role in endothelial function and inflammation is a critical factor in this context. The study conducted by Resnick et al. in the year 1992 emphasized that magnesium deficiency leads to endothelial dysfunction, a precursor to vascular complications in diabetes. This dysfunction, coupled with chronic inflammation, contributes to the progression of microvascular complications[14]. The present study findings are in line with this, indicating that patients with lower magnesium levels are more susceptible to these complications. Therefore, maintaining adequate magnesium levels could play a preventive role. Serum magnesium levels were also analyzed, revealing a noteworthy correlation with both glycemic control and the presence of microvascular complications. Participants with poor glycemic control and those with microvascular complications had significantly lower serum magnesium levels compared to those with good glycemic control and without complications. This suggests that hypomagnesemia may be a marker of poor glycemic control and a risk factor for developing microvascular complications in

diabetic patients. The strong correlation (r=0.840, p=0.0001) between low serum magnesium levels and microvascular complications highlights the potential role of magnesium in the pathophysiology of diabetes and its complications. These findings have important clinical implications. They suggest that regular monitoring of serum magnesium levels could be a valuable addition to the routine care of diabetic patients, particularly those struggling with glycemic control or at risk for microvascular complications. Moreover, addressing hypomagnesemia through dietary modifications or supplementation may be a potential therapeutic strategy to improve outcomes in this population.

CONCLUSION

This study highlights the critical role of serum magnesium levels in managing Type 2 diabetes mellitus, particularly concerning glycemic control and microvascular complications. Patients with poor glycemic control had significantly lower magnesium levels, which correlated with a higher incidence of complications such as retinopathy, nephropathy and neuropathy. These findings suggest that hypomagnesemia may be a marker of poor glycemic control and a risk factor for complications. Regular monitoring and potential supplementation of magnesium could improve patient outcomes, underscoring the importance of comprehensive diabetes management strategies that include micronutrient assessment.

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