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Study of Serum Magnesium Levels and Its Correlation with Glycated Haemoglobin Levels in Type 2 Diabetes Mellitus

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Abstract: ***Background:*** *Diabetes Mellitus is a metabolic disease with a very high incidence among Indian population. Diabetes Mellitus affects almost all body systems causing various structural and biochemical changes. Magnesium plays a key role in the metabolism of carbohydrates. It is mainly involved in diverting assimilable glucose for utilisation. This study is an attempt to find out the correlation between HbA1c (glycated hemoglobin) levels and serum magnesium levels in type-2 Diabetes Mellitus.* ***Aim:*** *To study the correlation between serum magnesium and glycated hemoglobin (HbA1c) levels in type-2 Diabetes Mellitus.* ***Materials and Methods:*** *130 people with type-2 Diabetes Mellitus and 130 normal healthy people without Diabetes were selected for the study. The age group of the study subjects were (30-55) years. Both fasting and post prandial blood samples were collected from both the groups and the blood samples were used for fasting blood sugar, HbA1c, serum magnesium and post prandial blood sugar determination.* ***Data analysis:*** *Data was analysed and expressed in terms of Mean ± SD. Unpaired student's t-test was used to compare the results between the diabetic and non-diabetic group. Pearson's correlation coefficient was used to find out the correlation between serum Magnesium and HbA1c levels in type-2 Diabetic patients.* ***Results:*** *Serum magnesium levels were significantly decreased ($p < 0.001$) in the type 2 Diabetic patients when compared to the non Diabetic control group. Mean serum magnesium values were (1.88± 0.28) in the type 2 Diabetic patients when compared to (2.1± 0.29) in the non Diabetic control group. There was also a statistically significant negative correlation ($r = -0.731$, P-value= 0.00) between HbA1c and serum magnesium levels in patients with type-2 Diabetes Mellitus.* ***Conclusion:*** *Serum magnesium levels show a strong negative correlation with HbA1c levels in type 2 Diabetic patients and thus, hypomagnesemia is commonly observed in type-2 Diabetes Mellitus with poor glycemic control.*

Keywords: *Correlation, Glycated Hemoglobin (HbA1c), Serum Magnesium, type-2 Diabetes Mellitus*

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I. Introduction

The number of people affected by Diabetes Mellitus is on the increase throughout the world. The total number of people affected world-wide by type-2 Diabetes Mellitus was expected to increase from 171 million in the year 2000 to 366 million by the year 2030 [1]. According to the data from International Diabetes Federation (IDF); the prevalence of the disease has already reached 366 million in the year 2011. The recent projections are that, the prevalence of Diabetes could well go beyond 438 million people being affected world-wide by the year 2030 [2]. Diabetes is associated with reduced life expectancy. Significant morbidity associated with Diabetes arises from microvascular complications and an increased risk of developing macrovascular complications [3].

Glycated Hemoglobin (HbA1c) was first identified by Allew, Schroeder and Balog in the year 1958 [4]. HbA1c is formed by the non-enzymatic reaction of glucose with the N-terminal Valine of the beta chain of hemoglobin [5]. Determination of HbA1c levels gives better information regarding Diabetic control. HbA1c values are free of day to day glucose variations and are unaffected by recent physical activity and food intake [6]. Measuring Glycated Hemoglobin (HbA1c) helps in monitoring the response to treatment in a diabetic patient [7]. HbA1c testing requires only a single blood sample and can be done once in three months [8]. The International Diabetic Federation and American College of Endocrinology has recommended HbA1c values below 6% as normal [9].

Magnesium is involved in glucose homeostasis. Magnesium is a critical cofactor for activities of various enzymes involved in glucose transport and glucose oxidation. Intracellular magnesium plays a key role in regulating Insulin action and Insulin mediated glucose uptake. Alteration in the metabolism of trace elements like magnesium is associated with Diabetes Mellitus [10]. Reduced serum magnesium levels has been documented in Diabetes Mellitus [11,12]. The possible causes of low serum magnesium levels in type-2 diabetic

patients are; osmotic diuresis causing high renal excretion of magnesium due to hyperglycemia, insensitivity to Insulin which affects intracellular magnesium transport with increased loss of intracellular magnesium [13] and reduced tubular reabsorption of magnesium due to Insulin resistance [14]. Decreased intracellular magnesium results in defective tyrosine kinase activity of the Insulin receptor and worsening of Insulin resistance in type-2 Diabetic patients [15,16].

Hypomagnesemia in type-2 Diabetes Mellitus also increases the risk of developing Diabetic complications like Diabetic nephropathy, neuropathy, retinopathy, dyslipidemia and diabetic foot ulcers [17].
The purpose of this study is to study the correlation between serum magnesium and glycated hemoglobin (HbA1c) levels in patients with type-2 Diabetes Mellitus. This is to demonstrate, how glycemic control in Diabetes can influence serum magnesium levels in type-2 Diabetic patients.

II. Materials and Methods

Study population

The study population included two groups of people. The first group included patients with type-2 Diabetes Mellitus (n =130). The second group consisted of healthy non-Diabetic people (n =130) which formed the comparative group.

Inclusion criteria

130 type-2 Diabetic patients of age group (30-55 years) with disease duration of less than 5 years who came for routine health check up to the medicine op of Govt. Kanyakumari Medical College Hospital, Asaripallam were recruited for the study. Another 130 normal healthy people without Diabetes formed the non-Diabetic group. They were taken from the people coming for routine health check up to the master health op.

Exclusion criteria

Patients with known history of (cardiovascular disease, respiratory disease, skeletal muscle injury, renal failure) terminally ill patients and chronic alcoholics were excluded from the study.

Blood Parameters studied

Serum Magnesium, Glycated Hemoglobin (HbA1c), Fasting Blood Sugar (FBS), Post Prandial Blood Sugar (PPBS)

Study method

Ethical committee clearance was obtained from the Human Ethical Committee, Govt. Kanyakumari Medical College Hospital, Asaripallam. Written informed consent was obtained from all the participants for the study. Details of the participants were recorded in a case record form. All the participants of the study were clearly explained about the study procedure. 5 ml of peripheral venous blood was obtained from the antecubital vein of the fore- arm from both the diabetic and non-diabetic group under strict aseptic conditions in the fasting and postprandial state. This sample was divided into two portions. The first part (2ml) was immediately transferred to an EDTA tube and used for HbA1c analysis. The second part (3ml) was collected in a red capped (plain tube) and allowed to clot for 3 minutes at room temperature and then centrifuged for 10 minutes. After separation, the serum samples were used for magnesium, fasting blood sugar and post prandial blood sugar determination.

The collected blood samples were assayed in the Central Lab of Biochemistry, Govt. Kanyakumari Medical College Hospital, Asaripallam. HbA1c percentage was analysed by Particle Enhanced Immuno-Turbidimetric test method using HbA1c XL System Pack kit. EM-360 Fully automated clinical chemistry analyser was used for HbA1c determination. Serum Magnesium was assayed by Arsenazo-III method. Fasting and Post Prandial Blood Glucose were determined by Glucose-Oxidase-Peroxidase enzymatic kit method. Erba Chem 5 plus V2 Semi automated clinical chemistry analyser was used for fasting blood glucose, post prandial blood glucose and serum magnesium measurements.

Statistical method of analysis

Statistical analysis was done using SPSS statistical package version 21. Data was expressed in terms of Mean ± SD. Comparison of results between the diabetic and non-diabetic group was done by unpaired student's t-test. Pearson's correlation coefficient was used to find out the correlation of serum Magnesium with HbA1c levels in type-2 Diabetic patients. Statistically significant variation was considered when p value was less than 0.05.

III. RESULTS

Table-1. Comparison of mean values of HbA1c and serum Magnesium between Diabetic and non-Diabetic control group

Variable	Diabetic Group (n= 130)	Non-Diabetic Group (n= 130)	Overall	P-Value
HbA1c (%)	8.41± 1.45	5.37± 0.29	6.89± 1.85	0.000**
Serum Magnesium (mg/dL)	1.56± 0.21	1.97± 0.15	1.76± 0.27	0.000**
FBS (mg/dL)	193.39± 58.22	89.44± 10.98	141.41± 66.78	0.000**
PPBS (mg/dL)	255.48± 70.24	111.11± 6.41	183.30± 87.80	0.000**

** - Highly Significant ($p < 0.001$) * - Significant ($p < 0.05$)

FBS - Fasting Blood Sugar; PPBS – Post Prandial Blood Sugar; HbA1c – Glycated Hemoglobin

Table-1 shows that there was a statistically significant decrease in the mean values of serum magnesium in the Diabetic group when compared to the non-Diabetic control group (P-value< 0.001); while, mean values of HbA1c, FBS and PPBS were significantly higher in the Diabetic group (P-value< 0.001).

Table-2. Correlation between HbA1c and serum Magnesium levels in Diabetic Group

		Serum Magnesium (mg/dL)
HbA1c (%)	Pearson correlation	-0.731**
	Sig.(2-tailed)	0.00
	N	130

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

Table-2 shows a strong negative correlation between HbA1c and Serum Magnesium levels in the Diabetic group (r = -0.731, P-value= 0.00).

Table-3. Comparison of mean values of HbA1c and serum Magnesium between Diabetic and non-Diabetic group in Males

Variables	Diabetic Group (Males)	Non Diabetic Group (Males)	P- Value
	N= 65	N= 65	
HbA1c (%)	8.20± 1.35	5.35±0.30	0.000**
Serum Magnesium (mg/dL)	1.56± 0.21	1.96 ±0.15	0.003*

** - Highly Significant ($p < 0.001$) * - Significant ($p < 0.05$)

Table -3 shows that Diabetic males had statistically significant decrease in mean serum magnesium levels with (P-value< 0.05) and statistically significant increase in mean HbA1c levels with (P-value< 0.001) when compared to non-Diabetic males who served as controls.

Table-4. =Comparison of mean values of HbA1c and serum Magnesium between Diabetic and non- Diabetic group in Females

Variables	Diabetic Group (Females)	Non Diabetic Group (Females)	P- Value
	N= 65	N= 65	
HbA1c (%)	8.20± 1.35	5.35±0.30	0.000**
Serum Magnesium (mg/dL)	1.57± 0.21	1.98 ±0.14	0.005*

** - Highly Significant ($p < 0.001$) * - Significant ($p < 0.05$)

Table- 4. Diabetic Females also showed a statistically significant rise in the mean HbA1c levels with (P-value< 0.001) and statistically significant decrease in mean values of serum magnesium with (P-value< 0.05) when compared to non-Diabetic Females who served as controls.

Table-5. Comparison of mean values of HbA1c and serum Magnesium between males and females in the Diabetic group

Variables	Diabetic Group (Males) N= 65	Diabetic Group (Females) N= 65	P- Value
HbA1c (%)	8.61± 1.52	8.20±1.35	0.10
Serum Magnesium (mg/dL)	1.56± 0.21	1.57 ±0.21	0.78

** - Highly Significant ($p < 0.001$) * - Significant ($p < 0.05$)

Table-5 shows that there was no statistically significant difference in mean values of HbA1c (P-value=0.10) and Serum Magnesium levels (P-value=0.78) between Males and Females in the Diabetic group.

Figure-1 Bar Diagram showing comparison of mean values of HbA1c and serum Magnesium Between Diabetic and non- Diabetic group

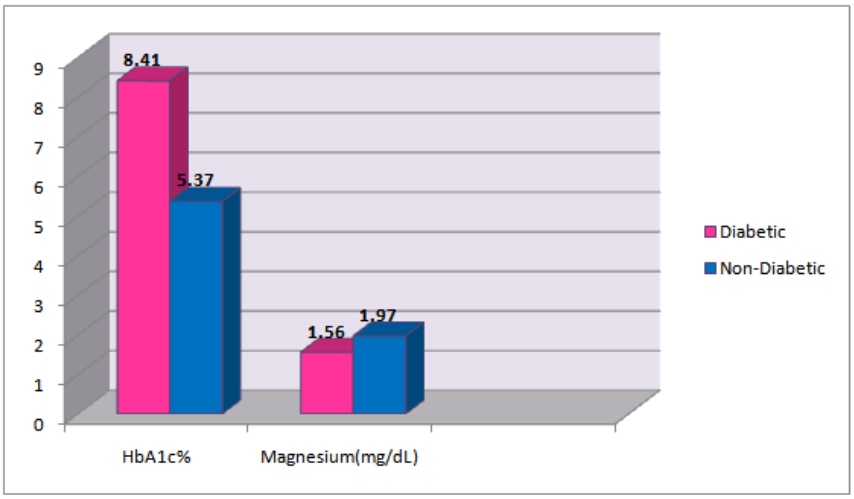

Figure-1. Bar Diagram illustrates decrease in the mean values of Serum Magnesium and increase in mean HbA1c levels in the Diabetic group when compared to the non-Diabetic control group.

Figure-2. Scatter diagram showing the Correlation between HbA1c and serum Magnesium levels in Diabetic Group

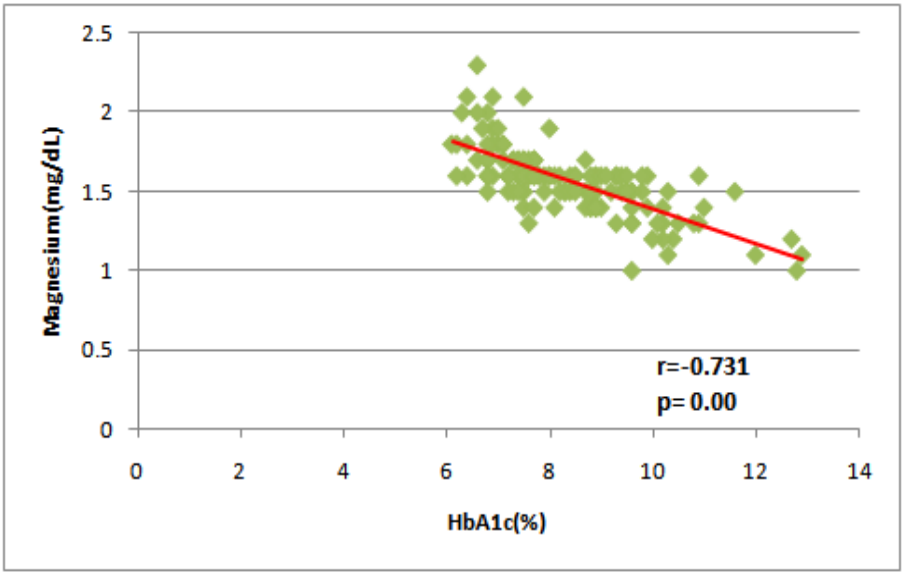

Figure-2. Scatter diagram shows that HbA1c levels are strongly negatively correlated with Serum Magnesium levels in the Diabetic group (r = -0.731, P-value= 0.00).

IV. Discussion

Results in our study (table-1 and figure-1) illustrate that, the mean values of serum magnesium were significantly decreased ($p < 0.001$) in patients with type-2 Diabetes Mellitus (1.56± 0.21) when compared to the healthy non-Diabetic controls (1.97± 0.15). In our study, the mean values of HbA1c in patients with type-2 Diabetes Mellitus was (8.41± 1.45) and they were significantly increased ($p < 0.001$) than those of the non-Diabetic controls with mean HbA1c values (5.37± 0.29). Similar findings were also observed in another study done by Rajendra Prasad et al [18]. who showed statistically significant decrease ($p < 0.001$) in mean values of serum magnesium in type 2 Diabetic patients (1.88± 0.28) when compared to non-Diabetic controls (2.1± 0.29). The findings in our study were also in accordance with another study done by Asha S Khubchandani and Hiren Sanghani [19] who showed statistically significant increase in mean values of HbA1c ($p < 0.01$) and statistically significant decrease in mean values of serum magnesium ($p < 0.01$) in patients with type-2 Diabetes Mellitus when compared to the healthy non-Diabetic controls. However, in contrast to our study, Naila M et al [20] did not show any statistically significant difference in serum magnesium levels in type 2 Diabetic patients when compared to the healthy non-Diabetic control group ($p > 0.05$).

The decrease in serum magnesium levels observed in type 2 Diabetic patients in our study may be due to poor glycemic control as shown by the increase in HbA1c levels. In type 2 Diabetic patients with magnesium deficiency, intracellular calcium levels are increased. Increased intracellular calcium levels interrupts Insulin mediated response on the skeletal muscle and adipose tissue and aggravates Insulin resistance [21]. Hypomagnesemia in type 2 Diabetic patients further impairs glycemic control by inducing altered cellular glucose transport, reducing pancreatic Insulin secretion, decreasing post receptor Insulin signalling and altering Insulin receptor interactions.

In our study, we have found a statistically significant negative correlation between HbA1c and serum magnesium levels (r = -0.731, P-value= 0.00) in patients with type-2 Diabetes Mellitus as shown under (table-2 and figure-2). The findings in our study are in agreement to another study done by Nehal EL Said et al [22]. who also showed statistically significant negative correlation between HbA1c and serum magnesium levels in patients with type-2 Diabetes Mellitus ($p < 0.001$). But, in contrast to our study, Walti MK et al [23]. did not show any statistically significant negative correlation between HbA1c and serum magnesium levels in type 2 Diabetic patients ($p > 0.05$).

In our study, there was no statistically significant difference in the mean values of serum magnesium and HbA1c between males and females in patients with type-2 Diabetes Mellitus ($p > 0.05$) as shown in (table-5). This finding is in accordance with another study done by Subrada Halder et al. [24] in type 2 Diabetic patients who also did not show any statistically significant difference in the mean values of serum magnesium and HbA1c with sex ($p > 0.05$).

V. Conclusion

In this study, we have documented a strong negative correlation between HbA1c and serum magnesium levels in patients with type-2 Diabetes Mellitus. We therefore conclude that, good glycemic control in type 2 Diabetic patients will significantly improve the serum magnesium levels and in turn reduce the risk of development of associated diabetic complications. We also recommend periodical monitoring of serum magnesium levels in type 2 Diabetic patients and whenever needed, proper supplementation of magnesium has to be considered.

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