# Study of Serum Magnesium and Its Correlation with HbA1c in Patients with Type 2 Diabetes Mellitus

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**ABSTRACT**

**BACKGROUND**
The metabolic dysregulation associated with DM causes secondary pathophysiological changes in multiple organ systems. We wanted to estimate the levels of serum magnesium and HbA1c in type 2 diabetes mellitus patients, study the correlation between serum magnesium and glycaemic control in these patients and evaluate the relation between serum magnesium and duration of diabetes in patients with type 2 diabetes mellitus.

**METHODS**
This is a cross sectional study of 160 cases conducted during between February 2017 to September 2018, in KIMS Hospital Hubli.

**RESULTS**
Out of 160 cases, 42% had hypomagnesemia whereas only 3% of the control group had low levels of magnesium. Mean value of magnesium was found to be lower in patients with diabetes of duration >10 years (1.4 mg/dL), whereas magnesium mean value was 2.1 mg/dL in patients with diabetes duration <5 years. Study results showed significant negative correlation between HbA1c, FBS, PPBS and serum magnesium. Mean magnesium level in the study group with HbA1c of more than 10 and less than 8 was 1.2 mg/dL and 2.0 mg/dL respectively. Magnesium levels were comparatively low in patients who were on insulin therapy.

**CONCLUSIONS**
Hypomagnesemia was more common in diabetes patients, especially in patients with longer duration of the disease. Lower magnesium levels were associated with poorer glycaemic control.

**KEYWORDS**
Type 2 Diabetes Mellitus, Insulin Resistance, Glycaemic Control, Serum Magnesium, HbA1c

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## BACKGROUND

Diabetes mellitus (DM) refers to a group of common metabolic disorders that share the phenotype of hyperglycaemia.[1] several distinct types of DM are caused by a complex interaction of genetics and environmental factors. Depending on the aetiology of the DM, factors contributing to hyperglycaemia include reduced insulin secretion, decrease glucose utilization, and increased glucose production. The metabolic dysregulation associated with DM causes secondary pathophysiological changes in multiple organ systems that impose a tremendous burden on the individual with diabetes.

### Disease Burden

Incidence of diabetes is increasing in Asian countries than other regions. The global burden due to diabetes is mostly contributed by type 2 diabetes which Constitutes 80% to 95% of the total diabetic population. Diabetes mellitus is the most Common metabolic disease and is a major public health challenge of the twenty-first Century. The explosive increase in the prevalence of diabetes seen in the last three decades Poses huge clinical and economic burden in many countries. Nearly 70% of the people with diabetes live in Developing countries; the largest numbers are in the Indian subcontinent and China.[2] The cost of diabetes care is high and is escalating worldwide. Due to rapid increase in the number of diabetics in the country India is called as the Global capital of diabetes.[3]

Among intracellular ions, magnesium has a major role in tyrosine kinase activity at Insulin receptor level and also at the post insulin receptor level of action of insulin. Magnesium has a major role in carbohydrate metabolism. It mainly acts as a cofactor for glucose transportation across the cell membrane, glucose oxidation and also in the Release of insulin. Deficiency of magnesium may lead to disturbance in glucose Metabolism and also at various levels of insulin secretion and its function. Reduced Intracellular magnesium concentration leads to reduced tyrosine kinase activity and Worsening of insulin resistance in diabetes mellitus. Hence detection of magnesium Levels in diabetic patients and treatment of hypomagnesemia is very important.[4,5] In T2DM, the prevalence of hypomagnesemia ranges between 14 and 48% compared with between 2.5 and 15% in healthy control subjects. Hypomagnesemia is associated with a more rapid, and permanent, decline in renal function in patients with T2DM.[6] In addition, epidemiological studies consistently show an inverse relationship between dietary intake and risk of developing[7] T2DM Several patient studies have shown beneficial effects of supplementation on glucose metabolism and insulin sensitivity.[8,9,10] Rodríguez-Morán et al.[11] published an excellent overview of the clinical studies addressing the role of magnesium in T2DM.

### Objectives

- To estimate the levels of serum magnesium and HbA1c in type 2 diabetes mellitus and to study the correlation of serum magnesium and HbA1c in these patients.
- To study the relation between duration of diabetes and serum magnesium levels in type 2 diabetes mellitus.

## METHODS

The study was carried out in Karnataka Institute of Medical Sciences, Hubli, Hospital OPD, from February 2017 to September 2018 among patients diagnosed with type 2 diabetes.

### Methods of Data Collection

Cases- patients with type 2 diabetes. Cases are divided in 3 groups according to the duration of diabetes Controls healthy individuals in the age group 30 or above. The study was approved by the institutional Ethics committee. A written informed consent was obtained from all participants in this study. The diagnosis of type 2 diabetes mellitus was confirmed by biochemical investigations.

Diagnosis of Type 2 DM was based on the American Diabetes Association criteria and clinical history as follows.

1. FBS≥ 126 mg/dL, OR
2. Symptoms of hyperglycaemia and RBS ≥200 mg/dL, OR
3. 2-hour plasma glucose ≥200 mg/dL after a 75 grams oral glucose tolerance test (performed as described by the World Health Organization), OR
4. On oral hypoglycaemic agents.

### Sample Size

Cases 160 patients were included as patients and 75 as controls. All the individuals in study were evaluated with detailed history, clinical examination and lab investigations which included-

- Structured proforma containing detailed history with diet history, duration of disease, treatment & co-morbidities.
- Detailed general and systemic examination.
- Fundus examination.
- Urine protein creatinine ratio.
- Blood samples for magnesium, HbA1c, lipid profile, RFT, FBS, PPBS, CBC.

### Inclusion Criteria

Patients with type 2 DM attending KIMS OPD who gave consent for the study are Included are included in the study.

### Exclusion Criteria

- Patients with acute or chronic diarrheal/ malabsorption syndrome
- Adrenal dysfunction,

- History of alcohol intake.
- History of vitamin or mineral supplements in the recent past.
- Pregnancy and lactation.
- History of vitamin or mineral supplementation
- Chronic kidney disease, nephrotic syndrome.
- Taking drugs known to affect magnesium level history of alcohol intake.
- Ethanol, Diuretics (loop, thiazide, osmotic) Cisplatin, Pentamidine, foscarnet.
- Cyclosporine, Aminoglycosides, Proton pump inhibitors, Amphotericin B.

**Statistical Methods**

Appropriate statistical tests of significance were applied and correlation between Variables were evaluated and the results were obtained which is being presented further.

## RESULTS

| | Cases | Controls |
|---|---|---|
| Total no. of subjects | 160 | 75 |
| Male | 86 | 41 |
| Female | 74 | 34 |
| Mean age | 56.2 | 54.8 |
| Mean duration of diabetes | 5.8 years | - |
| Mean magnesium (mg/dL) | 1.86 | 2.2 |
| Mean HbA1c% | 7.95 | 5.26 |
| Mean HDL (mg/dL) | 45 | 65.4 |
| Mean LDL (mg/dL) | 103.5 | 95.3 |
| Mean TGs (mg/dL) | 63 | 92 |
| Mean cholesterol (mg/dL) | 162 | 142 |
| Mean FBS (mg/dL) | 151 | 81 |
| Mean PPBS (mg/dL) | 213 | 120 |

***Table 1. Mean Values of Different Variables in Cases and Controls***

Among the study group 86 cases were males and 74 were females. Mean age in the study population was 56.2 years. Youngest case was 34 years and eldest was 80 years old. 80% of the study population was in the age group of 46-60 years in both males and females. Among the control group 41 were males and 34 were females. Mean age in the control group was 54.8 years. Mean magnesium in cases was 1.86 and in controls 2.2 mg/dL.

Mean magnesium levels were found to be lower in older patients. Magnesium level below the lower normal limit was found in 8 out of 28 patients in the age group of 30-45 years. Hypomagnesemia was found in 31 out of 76 patients in the age group of 46-60 years. Hypomagnesemia was found in 27 out of 54 patients in the age group of 61-75 years. But these results were not statistically significant.

Mean serum magnesium in the study group was found to be 1.86 mg/dL. Total 42% of the diabetic patients had magnesium levels below the normal range. Lowest value of magnesium being 0.8 and highest being 3.0 mg/dL. 54% of the cases had diabetes duration of <5 years in the study, and the mean magnesium level in this group was 2.1 mg/dL. 32% cases were diabetic since 5 to 10 years with mean magnesium level of 1.7 mg/dL. And 14 % of the cases belonged to the group of diabetes duration >10 years who had mean magnesium level of 1.4 mg/dL.

Association between serum magnesium and lipid profile was found only for HDL cholesterol. In our study 11% of patients were on insulin, 13% were on both insulin and OHA and 85% of the patients were on OHAs metformin being the most commonly used OHA. The mean magnesium in patients who were on OHAs was 1.9 and mean magnesium in patients who were on insulin was 1.6 and mean magnesium in patients who were on both insulin and OHA was 1.78.

## DISCUSSION

Patients with hypomagnesemia show a more rapid disease progression and have an increased risk for diabetes complications. Clinical studies demonstrate that T2DM patients with hypomagnesemia have reduced pancreatic b-cell activity and are more insulin resistant. Moreover, dietary supplementation of magnesium for patients with T2DM improves glucose metabolism and insulin sensitivity. Intracellular Mg Regulates glucokinase, KATP channels, and L-type $Ca^2$+ channels in pancreatic b-cells, preceding insulin secretion. Moreover, insulin receptor autophosphorylation is dependent on intracellular magnesium concentrations, making it a direct factor in the development of insulin resistance. Conversely, insulin is an important regulator of magnesium homeostasis. In the kidney, insulin activates the renal $Mg^{2+}$ channel transient receptor potential melastatin type 6 that determines the final urinary magnesium excretion. Consequently, patients with T2DM and hypomagnesemia enter a vicious circle in which hypomagnesemia causes insulin resistance and insulin resistance reduces $Mg^{2+}$ serum concentrations. This Perspective provides a systematic overview of the molecular mechanisms underlying the effects of on insulin secretion and insulin signaling[4,5]

In our study among the cases 86 were males and 74 were females. Mean age in the Study population was 56.2 years. Mean age in the control group was 54.8 years.

| Study | Mean Age | No. of Males | No. of Females |
|---|---|---|---|
| Our study | 56.2 | 86 | 74 |
| Ramachandra study[13] | 56.8 | 31 | 19 |
| Arundhat Dasgupta study | 51.4 | 93 | 57 |
| NH Rekha study[14] | 54.2 | 110 | 90 |
| Yeluri Sheshagiri Rao[15] study | 54.9 | 46 | 81 |

***Table 2. Age and Sex Distribution of Study Group in Other Studies***

**Comparison of Serum Magnesium and Duration of Diabetes**

Mean serum magnesium in the study group was found to be 1.86 mg/dL. Total 42% of the diabetic patients had magnesium levels below the normal range. Which is Consistent with findings in other studies. Lowest value of magnesium being 0.8 and Highest being 3.0 mg/dL. 54% of the cases had diabetes duration of <5 years in the study,

and the mean magnesium level in this group was 2.1 mg/dL. 32% cases were Diabetic since 5 to 10 years with mean magnesium level of 1.7 mg/dL. And 14% of the Cases belonged to the group of diabetes duration >10 years who had mean magnesium Level of 1.4 mg/dL. This finding of lower magnesium levels in patients with longer duration of diabetes was statistically significant and is consistent with other studies.

| Study | Mean Duration of Diabetes in Years | Mean Magnesium | Prevalence of Hypomagnesemia % |
|---|---|---|---|
| Our study | 5.79 | 1.86 | 42 |
| Ramachandra study | 3.58 | 1.92 | 28.4 |
| Arathi Ganiger study[16] | 12 years | 2.01 | 21.9 |
| NH Rekha studystudy | - | 1.7 | 57.7 |
| Yeluri Sheshagiri Rao study | 8.7 | 1.67 | 37.6 |

***Table 3. Comparison of Serum Magnesium***

| | Arathi Ganiger Study | | Ramachandra Study | | Yeluri Sheshagiri Rao Study | |
|---|---|---|---|---|---|---|
| | With Retinopathy (60) | Without Retinopathy (60) | With Retinopathy (25) | Without Retinopathy (25) | With Retinopathy (50) | Without Retinopathy (50) |
| Serum Mg | 1.9 | 2.1 | 1.4 | 1.9 | 1.3 | 1.67 |
| HbA1c | 7.7 | 7.3 | 9.9 | 8.9 | 7.7 | 7.3 |
| Duration of DM | 9.2 | 8.1 | | | 9.2 | 8.0 |
| FBS | 196 | 181 | 180 | 150 | 240 | 230 |
| PPBS | 240 | 230 | 264 | 255 | | |

***Table 4. Magnesium and Retinopathy***

| HbA1c | HbA1c <7 | 7-10 | >10 |
|---|---|---|---|
| Our study | 2.5 | 1.7 | 1.2 |
| Ramachandra study | 1.9 | 1.6 | 1.4 |
| Arundhati Dasgupta study | | 1.8 | 1.6 |
| Yeluri Sheshagiri Rao study | 1.84 | 1.67 | 1.42 |

***Table 5. Correlation between Magnesium and HbA1c***

**Comparison of Magnesium in Cases and Controls**

Study showed that serum magnesium was significantly lower in the diabetic patients compared to nondiabetics. Mean magnesium value in diabetics was 1.86 mg/dL and in non-diabetics was 2.2 mg/dL. This finding was consistent with the finding of greater prevalence of hypomagnesemia in diabetic patients. In a study done by N H Rekha, M S Bharath, S P Channakeshava, mean magnesium value in cases and controls was 1.7 mg/dL and 2.1 mg/dL respectively. Similarly mean magnesium in cases and controls was 1.67 and 2.07 respectively in the study done by Yeluri Sheshagiri Rao. In the study done by Arati Ganiger, K Mallikarjuna Swamy, Shivanand Gundalli mean magnesium levels in cases and controls was 2.07 and 2.71 respectively.

**Correlation between Magnesium and HbA1c**

Mean magnesium level in patients with HbA1c <7, 7-10, and >10% was 2.5, 1.7 and 1.2 respectively. This shows significant negative correlation between magnesium and HbA1c. The study done by Arundhati Dasgupta showed that the mean magnesium in patients with HbA1c 7-10 and >10% was 1.8 and 1.6 respectively. Similar results were obtained in the study done by Yeluri Sheshagiri Rao. In this study mean magnesium levels were 1.8, 1.6 and 1.42 for patients with HbA1c of <7, 7-10 and >10%. Hence our study showed lower magnesium level was associated with higher HbA1c levels. This result was statistically significant (p-<0.001) and consistent with other study results. In a study conducted by Ramachandra Prabhu H D, Shruti Kunche serum magnesium levels showed negative correlation with HbA1c. Another study conducted by Arundhati Dasgupta, Dipti Sarma, and Uma Kaimal Saikia mean HbA1c value for patients with normal magnesium level was 9.1 and for patients with hypomagnesemia was 11.9%.

**Serum Magnesium in Different Treatment Groups**

In our study 11% of patients were on insulin, 13% were on both insulin and OHA and 85% of the patients were on OHAs metformin being the most commonly used OHA. The mean magnesium in patients who were on OHAs was 1.9 and mean magnesium in patients who were on insulin was 1.6 and mean magnesium in patients who were on both insulin and OHA was 1.78.

In a study conducted by Yeluviri Sheshagiri Rao 49% of the patients were on insulin and their mean magnesium was 1.59, 33% of the patients were on OHAs and mean magnesium in this group was 1.95 and 18% of them were on combination of both OHA and insulin and mean magnesium in this group was 1.25. So mean magnesium was comparatively lower in patients who were on insulin. In a study conducted by Mohamed Murtuza Kauser, Asfia Afreen, Vageesh Kumar SR, out of the total of 50 diabetic patients, 25 (50%) were on insulin alone, 16 (32%) were on OHA'S and 9 (18%) were on combination of OHA'S and insulin. The mean serum magnesium levels in the OHA group, insulin group and the insulin+ OHA group were 2.02 mg/dL, 1.59 mg/dL and 1.25 mg/dL respectively. The serum magnesium levels were significantly lower in the insulin treated group compared to the OHA treated group.

**Magnesium and Proteinuria**

Studies have shown that hypomagnesemia was associated with increased risk of proteinuria specially microalbuminuria. Study done by Arundhati Dasgupta prevalence of micro and macroalbuminuria was more in patients with low magnesium levels. Ramachandra Prabhu also showed significant negative correlation between serum magnesium and albuminuria. In our study patients with proteinuria were excluded and negative correlation of hypomagnesemia and proteinuria in the form of raised urine albumin creatinine ratio was not statistically significant.

**Magnesium and Retinopathy**

In our study 9 patients had diabetic retinopathy mostly

nonproliferative diabetic retinopathy. Mean magnesium in this group was 1.52 mg/dL. Mean HbA1c was 8.6% in patients with retinopathy. Mean duration of diabetes was 11 years.

A total no. of 235 subjects was studied including 150 cases and 75 controls. both the groups were matched for age and sex distribution. The mean age in cases was 56.2 years and in controls 54.8 years. Among 160 cases 86 were males (51%), and among 75 controls 41 were males (54%).in the study group 70 out of 86 males were in the age group of 45-75 years. Similarly in control group 32 out of 41 males were in the age group of 30-60 years. 58 out of 74 female patients in the study group were in the age group of 45-75 years and among controls, out of 34 females 25 were in the same age group as in cases i e 45-75 years. Hypomagnesemia was more common in females.

Mean duration of diabetes was 5.9 years. 54% of the patients had diabetes since <5 years, 32.5% of them were diabetic for 5-10 years. The mean magnesium (mg/dL) was 2.1, 1.7, and 1.4 in patient groups of diabetes duration of less than 5 years, 5-10 years and more than 10 years respectively. The study showed that hypomagnesemia was more common in diabetic patients than control group. 42% of the patients had lower magnesium levels. Among the controls only 2 patients had low magnesium levels.

## CONCLUSIONS

Serum magnesium levels were lower in patients with poor glycaemic control as evidenced by higher HbA1c. Mean magnesium (mg/dL) in patients with HbA1c less than 6.9, 7-9, and more than 9 was 2.5, 1.75 and 1.2. Lower magnesium levels were also found in patients with higher FBS and PPBS levels. Patients who were on insulin therapy had lower magnesium levels than those who were on oral drugs.

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