

ORIGINAL RESEARCH

Study Of Correlation Between Serum Magnesium Level And Hba1c Level In Patient Of Type 2 Diabetes Mellitus Attending Medicine Department Of Tertiary Health Care

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ABSTRACT

Background: Magnesium deficiency at cellular level alters the membrane-bound Na⁺K⁺ AT Pase activity, which is essential for maintenance of sodium and potassium gradients in the transport of glucose. Hypomagnesemia has been linked with defective activity of tyrosine kinase which leads to impaired sensitivity of insulin receptors and exacerbates the insulin resistance among type 2 diabetics. This study was conducted to study serum magnesium levels and HbA1C levels in Type 2 DM patients and to study correlation between serum magnesium levels and HbA1C levels in Type 2 DM patients.

Methodology: This study was conducted as cross sectional study on diabetic patient reporting to medicine department during the study period of 18 months. Detailed history was obtained and clinical examination was done. CBC, FBS, PPBS and serum magnesium assessment was done in each patient.

Results: The present study was conducted on a total of 125 cases of type 2 diabetes mellitus with mean age of 57.82±10.14 years. Mean HbA1c in diabetic patients was 8.2±1.5% and majority of cases had serum magnesium levels above 1.6 mg/dl. Hypomagnesemia was significantly associated with increase fasting as well as post prandial blood glucose level (p<0.05). We observed a statistically significant very strong negative correlation of serum magnesium levels with serum HbA1c (r=-0.808, p<0.05) i.e. as the HbA1c increased, serum magnesium levels decreased significantly (p<0.05).

Conclusions: Hypomagnesemia is one of the common findings in patients with type 2 diabetes mellitus. Poor glycemic control as evidenced from increased FBS, PPBS and HbA1c have been associated with lower serum magnesium levels. As hypomagnesemia is linked with poor glycemic status, it may predict the complications among diabetic patients. It is recommended that serum magnesium levels must be monitored routinely in patients with diabetes as magnesium supplement may help in providing better glycemic control and preventing or delaying the progression of complications.

Keywords: hypomagnesimnia, glycemic index, HbA1c, blood glucose. Diabetes

INTRODUCTION

Diabetes is most common metabolic condition characterized by elevated blood glucose levels and may result from insufficient insulin production (due to inherited or acquired conditions)

or insulin resistance or both.^[1] Diabetes is a global public health problem, the prevalence of which is rising rapidly worldwide.^[2] According to International Diabetes Federation (2016), approximately 415 million adults are estimated to be suffering from diabetes globally, and this burden is projected to increase to 642 million by the year 2040.^[3] However, India is referred to as the diabetes capital of the world as India contribute to approximately 17% of the total cases of diabetes across the globe.^[4] In India, diabetes is expected to be affecting 69.9 million by 2025, which is further extrapolated to hit the alarming mark of 80 million by 2030, thus the burden is expected to increase by 266%.^[5]

The pathophysiological mechanisms of diabetes include deficient insulin secretion, resistance to the insulin action and increased gluconeogenesis. Glucose homeostasis i.e. tight regulation of blood glucose levels within the normal range is one of the most common strategy for reducing the acute and chronic complications associated with diabetes mellitus.^[6] Glucose increases the levels of intracellular calcium and decrease the levels of intracellular magnesium.^[7]

Magnesium, fourth most abundant trace mineral, is involved in numerous metabolic pathways in the body.^[8] Magnesium acts as cofactor in in more than 300 enzymes in various essential anabolic and catabolic processes such as ATP generation, muscle contraction, DNA replication & repair, signal transduction, blood pressure maintenance, carbohydrate oxidation, insulin secretion and glycemic control.^[9,10] Though the deficiency of magnesium is common in certain metabolic disorders including diabetes mellitus type 2, it is often undiagnosed.^[11] Overall, the prevalence of hypomagnesemia is reported to range from 44% to 65% in cases with type 2 diabetes.^[12,13]

Magnesium is an important cofactor which has significant impact on the glucose homeostasis and its depletion in cases with diabetes has negative impact on glucose homeostasis. Magnesium deficiency at cellular level alters the membrane-bound Na⁺ K⁺ATPase activity, which is essential for maintenance of sodium and potassium gradients in the transport of glucose.^[14] The negative impact of magnesium deficiency in glucose homeostasis could be attributed to decreased sensitivity of peripheral tissues to insulin leading to poor glycemic control, carbohydrate intolerance and development of diabetic complications.^[15]

Though the exact role of magnesium in pathogenesis of insulin resistance is unknown, however, hypomagnesemia has been linked with defective activity of tyrosine kinase which leads to impaired sensitivity of insulin receptors and exacerbates the insulin resistance among type 2 diabetics.^[16,17] The deficiency of magnesium in diabetes may aggravate acute and chronic complications associated with diabetes such as retinopathy, peripheral vascular disease, thrombosis etc.^[18] Literature suggest that magnesium deficiency may inhibit the entry of calcium into the myocardial cells leading to excess intracellular calcium levels and formation of crystals in mitochondria. These changes has been linked with increased cardiovascular morbidity in patients with type 2 diabetes.^[19] Previous studies have showed hypomagnesemia in significant proportion of patients with Type 2 DM.^[17,18] However, previous studies have mainly done on blood glucose levels, only limited data had been reported in our country based on the HbA1C level and magnesium level in type 2 DM. With the above background, the present study was conducted to study serum magnesium levels and HbA1C levels in Type 2 DM patients and to study correlation between serum magnesium levels and HbA1C levels in Type 2 DM patients.

METHODOLOGY

The present study was conducted as an observational cross sectional study on diabetic patient reporting to medicine department, PCMS & RC and People's Hospital, Bhopal during the study period of 18 months i.e. from 1st December 2020 to 31st May 2022. All diabetes mellitus patient attending medicine department were included whereas patients with renal failure, on

magnesium supplements since last 3 months, on diuretics, with chronic diarrhoea of more than 6 weeks and Pregnant women were excluded from the study.

The study was approved by Institute's ethical committee prior to its commencement. After obtaining written consent from the study participants fulfilling inclusion and exclusion criteria, patients were recruited in the study. Detailed data regarding the sociodemographic variables along with detailed history with respect to mode of presentation, duration of diabetes, diabetes treatment, presence of comorbidities was obtained using proforma. All the patients with type 2 diabetes were subjected to detailed clinical examination. Their vitals such as pulse rate, respiratory rate, blood pressure, temperature was recorded. Anthropometric measurements including their height, weight, and waist circumference was documented in proforma and BMI was calculated.

Thorough investigations were done in all the cases which included complete blood picture (using autoanalyzer), fasting and post prandial Blood Glucose and HbA1c. Apart from this, blood sample was subjected to serum magnesium assessment using "Roche cobas c311 analyzer".

STATISTICAL ANALYSIS

Data was compiled using MsExcel and analysed using IBM SPSS software version 20. Continuous variables were expressed as mean and standard deviation whereas categorical variables were expressed as frequency and proportions. Association of HbA1c with serum magnesium levels was observed using chi square test (for categorical variables- presence or absence of hypomagnesemia) and one way ANOVA (for continuous variables- mean magnesium levels). Serum magnesium levels were correlated with HbA1c levels using Pearson's Correlation coefficient. P value of less than 0.05 was considered significant.

RESULTS

The present study was conducted on a total of 125 cases of type 2 diabetes mellitus with mean age of 57.82 ± 10.14 years.

Table 1: Distribution of patients according to baseline variables

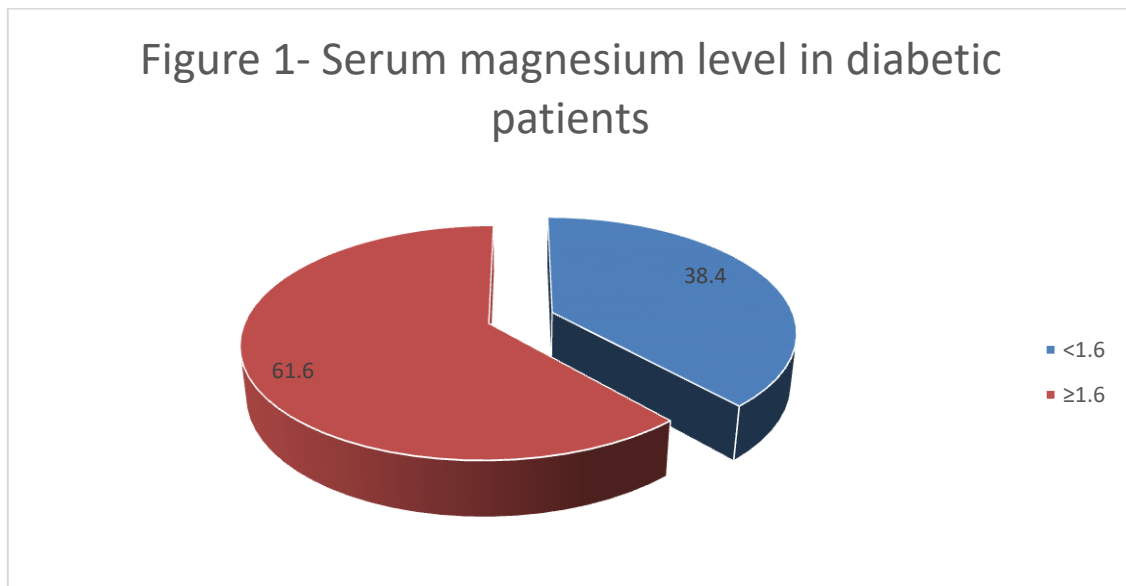
| Baseline variables | Frequency (n=125) | Percentage | |
|------------------------------|----------------------|------------|------|
| Age (years) | ≤45 | 14 | 11.2 |
| | 46-60 | 59 | 47.2 |
| | 61-75 | 45 | 36.0 |
| | >75 | 7 | 5.6 |
| Sex | Male | 60 | 48.0 |
| | Female | 65 | 52.0 |
| BMI (kg/m ²) | <18.5 (Underweight) | 0 | 0 |
| | 18.5-24.9 (Normal) | 80 | 64.0 |
| | 25-29.9 (Overweight) | 39 | 31.2 |
| | ≥30 (Obese) | 6 | 4.8 |
| Duration of diabetes (years) | ≤5 | 42 | 33.6 |
| | 6-10 | 60 | 48.0 |
| | >10 | 23 | 18.4 |

Majority of cases belonged to age group of 46 to 60 years (47.2%), and slight female predominance was noted in our study for diabetes, with male: female ratio of 0.92:1. Mean duration of diabetes was 7.52 ± 3.5 years and about 48% cases were suffering from diabetes since 6 to 10 years. Mean BMI of patients with diabetes was 24.55 ± 2.6 kg/m². About 31.2% cases were overweight and 4.8% patients were obese.

Table 2: Distribution according to blood glucose level and HbA1c

| Blood glucose | | Frequency (n=125) | Percentage |
|----------------------|---------|-------------------|------------|
| Fasting (mg/dl) | <140 | 35 | 28.0 |
| | >140 | 90 | 72.0 |
| Post prandial(mg/dl) | <200 | 44 | 35.2 |
| | >200 | 81 | 64.8 |
| HbA1c (%) | <6.5 | 6 | 4.8 |
| | 6.5-7.4 | 41 | 32.8 |
| | 7.5-8.4 | 37 | 29.6 |
| | 8.5-9.4 | 18 | 14.4 |
| | ≥9.5 | 23 | 18.4 |

Mean fasting and postprandial blood glucose levels were 173.7 ± 58.6 and 257.1 ± 90.9 mg/dl respectively. About 72% cases had fasting blood glucose above 140 mg/dl and 64.8% cases had post prandial blood glucose above 200 mg/dl. Mean HbA1c in diabetic patients was $8.2 \pm 1.5\%$, and HbA1c ranged between 6.5 to 7.4% in 32.8% cases.



Mean serum magnesium level in patients with diabetes was 1.9 ± 0.4 mg/dl, and majority of cases had serum magnesium levels above 1.6 mg/dl. About 38.4% cases had serum magnesium level below 1.6 mg/dl (hypomagnesemia) (Figure 1).

Table 3: Association of blood glucose level and HbA1c with serum magnesium levels

| Blood glucose (mg/dl) | Magnesium | | | | χ^2 | P value | |
|-----------------------|-------------|------------|-------------|------------|----------|---------|-------|
| | <1.6 (n=48) | | ≥1.6 (n=77) | | | | |
| | Frequency | Percentage | Frequency | Percentage | | | |
| Fasting | <140 | 1 | 2.1 | 34 | 44.2 | 25.9 | 0.001 |
| | >140 | 47 | 97.9 | 43 | 55.8 | | |
| Post prandial | <200 | 1 | 2.1 | 43 | 55.8 | 37.5 | 0.001 |
| | >200 | 47 | 97.9 | 34 | 44.2 | | |
| HbA1c | <6.5 | 0 | 0 | 6 | 7.8 | 72.9 | 0.001 |
| | 6.5-7.4 | 1 | 2.1 | 40 | 51.9 | | |
| | 7.5-8.4 | 11 | 22.9 | 26 | 33.8 | | |

| | | | | | | | |
|--|---------|----|------|---|-----|--|--|
| | 8.5-9.4 | 13 | 27.1 | 5 | 6.5 | | |
| | ≥9.5 | 23 | 47.9 | 0 | 0 | | |

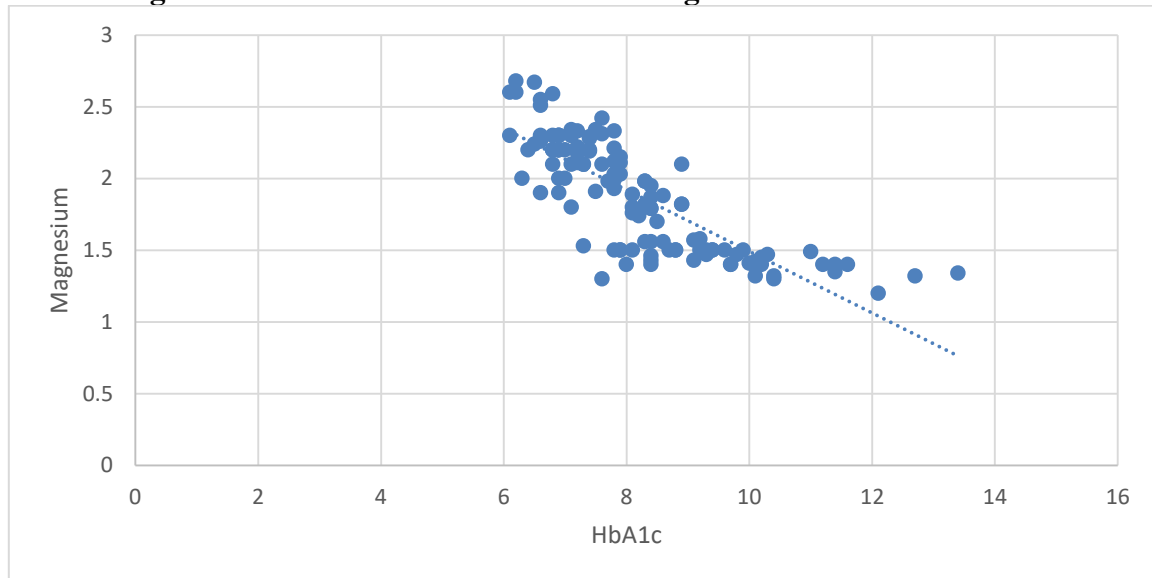
In present study, hypomagnesemia was significantly associated with increase fasting as well as post prandial blood glucose level ($p<0.05$). Majority of patients with normal serum magnesium levels had HbA1c below 7.5% (59.7%) whereas >95% cases with serum magnesium level below 1.6 mg/dl had HbA1c above 7.5%. We observed a statistically significant association of hypomagnesemia with raised HbA1c levels ($p<0.05$).

Table 4: Correlation between Serum magnesium and HbA1c levels

| R | R Square | Adjusted R Square | Std. Error of the Estimate | F | Sig. |
|--------|----------|-------------------|----------------------------|----------------|---------------|
| -0.808 | -0.653 | -0.650 | -0.230 | 231.594 | 0.0001 |

The present study reported a significantly very strong negative correlation of serum magnesium levels with serum HbA1c ($r=-0.808$, $p<0.05$) i.e. as the HbA1c increased, serum magnesium levels decreased significantly ($p<0.05$).

Figure 2: Correlation between Serum magnesium and HbA1c levels



DISCUSSIONS

Diabetes is a global public health problem which is characterized by altered glucose homeostasis due to impaired insulin secretion or action.^[6] This homeostasis of glucose is essential for maintaining the intracellular calcium and magnesium levels.^[7] The magnesium deficiency is documented in certain metabolic conditions including diabetes mellitus type 2, with reported hypomagnesemia in 44% to 65% of the cases.^[11-13] Reduced magnesium levels has negative impact on glucose homeostasis as hypomagnesemia alters the membrane-bound Na⁺ K⁺ ATPase activity and defective activity of tyrosine kinase which leads to impaired sensitivity of insulin receptors causing insulin resistance.^[14,16,17] The deficiency of magnesium in diabetes have been associated with increased microvascular as well as macrovascular complications associated with diabetes.^[19] This study was conducted on a total of 125 cases of type 2 diabetes mellitus to study correlation between serum magnesium levels and HbA1C levels in Type 2 DM patients. Mean age of patients with diabetes was 57.82±10.14 years with slight female predominance (52%).

Hypomagnesemia is commonly reported in patients with diabetes, and low concentration of serum magnesium further aggravates the insulin resistance and increases the risk of diabetic complications.^[14-17] The role of single nucleotide polymorphisms have been documented linking hypomagnesemia with type 2 diabetes.^[20] Apart from this, changes at the genetic level in the KATP channels of pancreatic beta cells have been postulated in insulin resistance and thus increasing diabetes risk.^[20]

In our study, mean serum magnesium levels among diabetic were 1.9 ± 0.4 mg/dl and we reported low serum magnesium levels in 38.4% diabetics. The findings of present study were supported by the findings of Kulkarni et al, in which 37% cases of diabetes had low serum magnesium levels and the hypomagnesemia was documented to be significantly higher among diabetics as compared to controls ($p < 0.05$).^[18] Mean serum magnesium levels in patients with diabetes was 1.79 ± 0.34 mg/dL in a study of Nawal et al and serum magnesium levels were lower in significantly higher proportions of cases with diabetes (47%) as compared to controls (6%) ($p < 0.05$).^[21] Patil et al also documented significantly lower serum magnesium levels in in diabetic cases (1.69 ± 0.29 mg/dl) as compared to controls (1.96 ± 0.18 mg/dl) ($p < 0.001$).^[22] Quidi et al documented hypomagnesemia in 14.56% patients with diabetes mellitus.^[12] About 44% cases with diabetes had hypomagnesemia in a study of Kumar et al.^[15]

Assessment of glycemic status was done using FBS, PPBS and HbA1c levels. Fasting blood glucose and post prandial blood glucose levels were raised in 72% and 64.8% cases whereas HbA1c ranged between 6.5 to 7.4% in 32.8% cases. Mean HbA1c levels among diabetic patients was $8.2 \pm 1.5\%$. We reported hypomagnesemia to be significantly associated with poor glycemic control i.e. with increased FBS, PPBS as well as HbA1c levels ($p < 0.05$). Also we reported a very strong negative correlation of serum magnesium levels with serum HbA1c ($r = -0.808$, $p < 0.05$) suggesting significant reduction in magnesium levels as the HbA1c levels increased. Our study findings were concordant with the findings of Patil et al), in which the authors documented significantly poor glycemic control (increased HbA1c) in diabetic patients with low serum Mg²⁺ levels as compared to those with normal glucose levels ($p < 0.05$).^[22] Mohammed et al documented a significant negative correlation of serum magnesium levels with fasting blood glucose and HbA1c, supporting our study findings ($p < 0.05$).^[23] Quidi et al reported a significant association between HbA1c levels and hypomagnesemia, along with a negative linear relationship of serum magnesium levels with fasting blood sugar levels as well as HbA1c.^[12] Our study findings were supported by findings of Paladiya et al, in which patients with poor glycemic control had significantly lower serum magnesium levels as compared to those with good glycemic control ($p < 0.05$).^[24] Moradiya et al also reported significantly lower serum magnesium levels in patients with poor glycemic control (HbA1c $\geq 7\%$) as compared with the patients with HbA1c below 7% along with a significant negative correlation of serum magnesium with HbA1c ($r = -0.499$; $P < 0.05$).^[25]

Thus hypomagnesemia is seen diabetic patients as a consequence of diabetes and may itself worsen the glycemic status of the diabetic patients.^[26] The exact cause of hypomagnesemia in diabetes is unclear, however, low dietary intake, increased urinary loss, or impaired magnesium absorption have been reported in patients with diabetes.^[27,28] Recently, the specific defect in renal tubules have been postulated which causes reduced reabsorption of magnesium in thick ascending loop of Henle, which is linked with hypomagnesemia.^[26] Magnesium act as cofactor in number of biochemical reactions including glucose transporting mechanisms. Magnesium deficiency alters the glucose transporting mechanism and promote insulin resistance, even in non diabetic patients.^[29]

CONCLUSIONS

Hypomagnesemia is one of the common findings in patients with type 2 diabetes mellitus. Serum magnesium levels are observed to be lower in patients with prolonged duration of diabetes and obese individuals. Poor glycemic control as evidenced from increased FBS, PPBS and HbA1c have been associated with lower serum magnesium levels. As hypomagnesemia is linked with poor glycemic status, it may predict the complications among diabetic patients. It is recommended that serum magnesium levels must be monitored routinely in patients with diabetes as magnesium supplement may help in providing better glycemic control and preventing or delaying the progression of microvascular as well as macrovascular complications.

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