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Original Article

Evaluation of serum magnesium levels in type 2 diabetes mellitus patients

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Abstract

Background: Magnesium is an abundant intracellular cation in humans. Magnesium is essential for insulin secretion and its effective action. Secretion of insulin by beta cells of pancreas depend on the regulation of ATP stimulated channels by magnesium. Magnesium is a cofactor for kinases which is responsible for the insulin action through receptors. Thereby hypomagnesemia can cause decreased uptake of glucose by the cells. Decreased serum magnesium levels in type 2 diabetes mellitus are documented in several studies. **Aim:** To observe the serum magnesium levels in type 2 diabetes patients in Tamil Nadu part of South India. **Settings and Design:** Study group includes 203 type 2 diabetic patients. Exclusion criteria are type 1 diabetes and chronic diseases. Age matched apparently 203 healthy individuals were selected as control group. **Materials and Methods:** Fasting blood glucose, serum magnesium and glycated haemoglobin were analyzed in the blood samples using standard kits. **Statistical analysis used:** Student's 't' test and correlation coefficient. **Result:** Serum magnesium levels were significantly lowered in the study group when compared with the control group ($p < 0.001$). We observed a negative correlation ($r = -0.163$, $p < 0.05$) between serum magnesium and glycated haemoglobin in the study group. **Conclusion:** The serum magnesium has been significantly lowered in type 2 diabetes patients. Hypomagnesemia in these patients may worsen the insulin resistance. Supplementing magnesium in these patients will help in reducing insulin resistance.

Key-words: Hypomagnesemia, Diabetes mellitus and Glycated haemoglobin.

Introduction

Magnesium (Mg) is the second most abundant intracellular cation next to potassium in the human body.[1,2] Magnesium is necessary for more than 300 biochemical reactions.[3] Enzymes which need magnesium as a cofactor are carboxylase, glucose 6 phosphatase, arginase, HMG CoA reductase. Magnesium act as an allosteric activator for enzymes like phosphofructokinase, ATPase, alkaline phosphatase.[1] Magnesium plays an important role in neuromuscular excitability and cell permeability.[4] Magnesium is also required for insulin secretion.[5] Pancreatic beta cell cycle requires magnesium for its maintenance. Extracellular magnesium may regulate the ATP sensitive potassium channels in the beta cells. This in turn increases the intracellular calcium levels. The increased intracellular calcium levels is responsible for the release of insulin from the storage granules.[6,7] Magnesium has a definite role in insulin hormone receptor interaction and favours the glucose entry into the cells.[5] Magnesium increases the body's ability to utilize calcium, phosphorus, sodium, vitamin C, vitamin E and vitamin B complex.[2] In the brain, magnesium is predominantly complexed with ATP. This ATP-Mg complex is required for cellular biological processes.[8] Diabetes mellitus is a disorder of heterogeneous etiology with absolute or relative deficiency of insulin and the common denominator is hyperglycemia.[9] Many studies show a close relationship between diabetes mellitus and magnesium deficiency.[10,11,12,13] A cross sectional study by Sharma. A et al in India reveals that hypomagnesemia occurs in both type 1 and type 2 diabetes patients.[14] Masood. A et al reported that decreased serum magnesium concentration was observed in type 2 diabetes patients compared to type 1 diabetes patients.[15] Few European studies have also documented low serum magnesium levels in diabetes mellitus.[16,17] K. Monika et al and K. Ueshima et al reported that hypomagnesemia is a strong independent predictor of type 2 diabetes.[18,19] In

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hypomagnesemic conditions, there is defective tyrosine kinase activity at the insulin receptor levels which results in impaired insulin interaction with the insulin receptor. This leads to worsening of insulin resistance.[20] However osmotic diuresis, hypolipidemic agents, etc will increase urinary excretion of magnesium, causing hypomagnesemia in diabetes. Therefore hypomagnesemia is a cause or consequence of diabetes mellitus.[21,22] Insulin regulates the intracellular magnesium concentration by stimulating ATP- Mg dependent calcium pump. [20] Milagros G Huerta et al reported that obese non diabetic children have lower serum magnesium concentration than lean non diabetic children.[23] Thus magnesium plays a salient role in the maintenance of normal body weight also.[24] Hypomagnesemia was observed in people with impaired fasting glucose.[25] Several studies have shown the association between hypomagnesemia and various complications of type 2 diabetes mellitus like neuropathy, retinopathy, foot ulcers, etc.[3,26] M. S. Ahmed Baig et al has shown a correlation between serum magnesium and severity of diabetes.[27] It was proposed to study the association between serum magnesium levels in type 2 diabetes patients in Tamil Nadu part of South India and to observe the relationship between serum magnesium and glycated haemoglobin in type 2 diabetes patients.

Materials and methods

The present study has been approved by Sri Ramachandra Institutional ethics committee. Individual informed consents was signed by the participants. The study comprises of 2 groups. Control group 203 age matched apparently healthy individuals were selected among the staffs of Sri Ramachandra Medical College and forms the control group. Staffs Master health checkup examination was took into consideration to identify individuals are healthy. Study group- 203 patients diagnosed with type 2 diabetes, aged 30 years and above of both gender were selected from diabetic department of Sri Ramachandra Hospital. Exclusion criteria for this group were patients having type 1 diabetes, hypertension, cancer, hyperthyroidism, pancreatitis, Cushing's disease, renal disease, cardiovascular disease, smokers and alcoholics. Blood samples were collected from both group participants (406) in the fasting state using vacutainers with and without anticoagulants (sodium fluoride and EDTA). These vacutainers were centrifuged at 3500 rpm for 10 minutes. The serum and plasma were separated and stored at -20•C. Before sample analysis, the frozen samples were thawed and then used for analysis. Following parameters were analyzed by the corresponding methods. Magnesium - Dye binding method (Reference range – 1.8 to 2.4 mg/dl) Glucose Hexokinase enzymatic method (Reference range 70 to 110 mg/dl) Glycated haemoglobin High performance liquid chromatography (Ref range – 4 to 6%) Glucose and magnesium were processed in Dimension RxL automated clinical chemistry analyzer using standard kits. Glycated haemoglobin was processed using standard kit in BioRad D-10 automated analyzer. The results of all the parameters were expressed as Mean ± Standard deviation. Statistical analysis were done by Student's 't' test and the p value was arrived to assess the statistical significance observed between two groups. The association between parameters were assessed by correlation coefficient.

Result

The results of our study are shown below:

Table 1. Demographical data and biochemical parameters in the control and study groups

Particulars	Control Group N = 203	Study Group N = 203
Gender (Male %)	67.5%	61.5%
Gender (Female %)	32.5%	38.4%
Age (in years)	51.8 ± 8.1	55.7 ± 10.7
Fasting blood glucose (mg/dl)	88.8 ± 10.6	155.8 ± 58.3***
Glycated haemogloin (%)	5.08 ± 0.57	8.3 ± 2.1***
Serum magnesium (mg/dl)	2.16 ± 0.1	2.08 ± 0.2***

***p < 0.001

Fig 1. Fasting blood glucose level in the present

In the present study at baseline, the study group had significantly high fasting blood glucose level and gyrated hemoglobin (p < 0.001) compared to control. As shown in table 1 and Fig 1 & 2 .

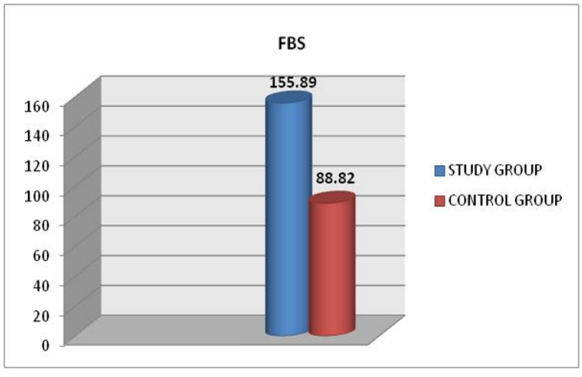


Fig 2. Glycated haemoglobin level

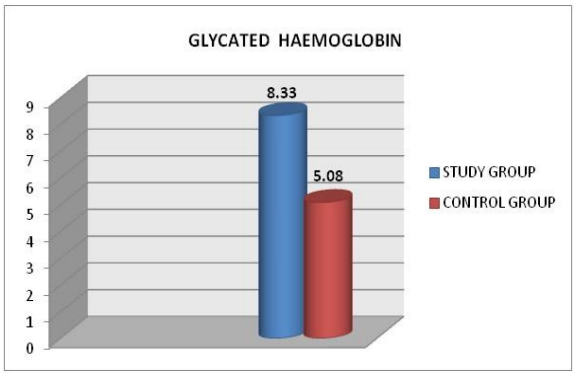
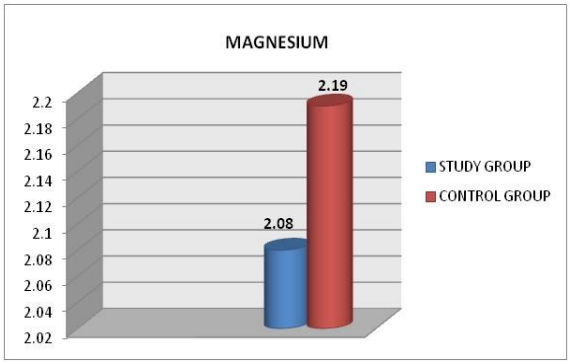
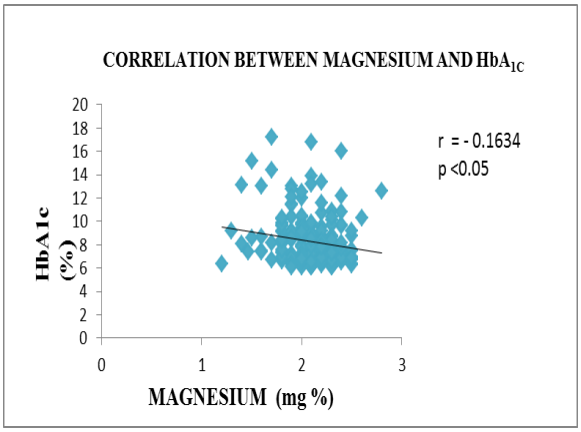


Fig 3. Serum magnesium level



We also observed a significantly low serum magnesium level ($p < 0.001$) in study group when compared with the control group (Fig 3).

Fig 4. Correlation between serum magnesium level and glycated haemoglobin in the study group



A negative correlation ($r = -0.1634$, $p < 0.05$) between magnesium and glycated haemoglobin was observed in the study group (Fig 4) but there was no correlation between serum magnesium and fasting blood glucose in the study group.

Discussion

In the present study, type 2 diabetes patients have low serum magnesium levels compared with controls. Several authors have documented similar results.[28,29,30,31] However Naila Masood et al and Abdul. H. Zargar et al had shown normal serum magnesium levels in type 2 diabetes mellitus.[32,33] Magnesium deficiency leads to decreased insulin sensitivity.[34] On the other hand, diabetes mellitus can cause hypomagnesemia. In uncontrolled diabetes mellitus, there is impairment of tubular reabsorption of magnesium and increased excretion of magnesium due to osmotic diuresis. Regulation of intracellular magnesium is insulin dependent. Therefore insulin resistance may lead to low serum magnesium levels.[35,36] There was no significant correlation between fasting blood glucose and serum magnesium levels. However a negative correlation between glycated haemoglobin and serum magnesium levels were documented in our study. The negative correlation between glycated haemoglobin and serum magnesium levels indicate that the long term control of blood glucose may be an important factor in maintaining serum magnesium levels. Under physiological conditions, glycated haemoglobin results from the non enzymatic glycosylation and depends on the blood glucose levels for the past three months.

Therefore glycated haemoglobin (HbA1c) is a better marker for the good control of blood glucose.[37,38] E. N. Esfahani et al had documented no correlation between fasting blood glucose and serum magnesium levels as in our study.[39] A negative correlation between serum magnesium and glycated haemoglobin in our study was similar to the results reported by M. Salem et al and Supriya et al.[40,41] Several authors documented that oral magnesium supplementation in type 2 diabetes patients had improved the insulin sensitivity and corrected hypomagnesemia.[42,43,44] P. Chaudhary et al had reported that in elderly individuals without diabetes, magnesium supplementation improved insulin sensitivity.[45]

Conclusion

The present study observed hypomagnesemia in type 2 diabetes patients from Tamil Nadu population in comparison with apparently healthy individuals. Hypomagnesemia can cause insulin resistance. Various factors like osmotic diuresis, hypolipidemic drugs in diabetes patients can lead to urinary magnesium excretion. Therefore magnesium deficiency can be both as a cause or consequence of diabetes mellitus. Our study suggest that diabetes patients may have better control of blood

glucose if magnesium is supplemented along with oral hypoglycemic agents. Further study should be done to find out whether magnesium deficiency is a cause or consequence of diabetes mellitus.

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