STUDY RELATED TO SERUM MAGNESIUM AND TYPE 2 DIABETES IN A SMALL GROUP OF PATIENTS ATTENDING MGMGH, TRICHY

Vijayalakshmi S[1], Arshiya Begum A[2], Nirmala Devi K[3], Srivatsan E[4], Latha J[5], Priya A[6], Saravanan B[7], Vanitha K[8]

[1]Assistant Professor, Department of Biochemistry, K. A. P. V. Government Medical College.
[2]Professor, Department of Biochemistry, K. A. P. V. Government Medical College.
[3]Professor, Department of Biochemistry, K. A. P. V. Government Medical College.
[4]Assistant Professor, Department of Biochemistry, K. A. P. V. Government Medical College.
[5]Tutor, Department of Biochemistry, K. A. P. V. Government Medical College.
[6]Tutor, Department of Biochemistry, K. A. P. V. Government Medical College.
[7]Tutor, Department of Biochemistry, K. A. P. V. Government Medical College.
[8]Assistant Professor, Department of Biochemistry, K. A. P. V. Government Medical College.

ABSTRACT

BACKGROUND: INTRODUCTION:

Diabetes mellitus and its complications are in an increasing trend and it is important to look for parameters which can detect early and delay the onset of disease as well as complications. Serum magnesium levels can be taken as one such indicator.

AIM

The aim of the study is to:

1) Estimate the level of serum magnesium levels in type 2 diabetic patients and controls.
2) Determination of the correlation between the level of serum magnesium in diabetics and nondiabetics.

MATERIALS & METHOD:

In this study, we have chosen a total of 100 subjects with 50 of them as nondiabetic controls and the rest 50 being diabetics taken as test group. We took fasting samples in all subjects and performed all the routine test parameters. In addition, we assayed the magnesium levels in all subjects.

RESULTS & STATISTICS:

The mean magnesium level for both groups were 2.6+/-0.37 and 1.1+/-0.38 in the nondiabetic control group and diabetic test group respectively (This is statistically significant and a student t test showed a t value of 7.589-E13 which corresponds to a p value <0.001-statistically significant).

CONCLUSION:

Thus, our study concluded that there is a significant low level of serum magnesium in diabetic patients which may be an important factor in early onset of the disease in susceptible individuals.

KEYWORDS:

Magnesium, Diabetes Mellitus, Study, Correlation.

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INTRODUCTION: Diabetes mellitus and the spectrum of clinical conditions associated with it has been under research for quite a number of years. During all these years there have been many changes and updates in the diagnostic aspects and treatment protocols based on the results of the various research papers published globally. Many new markers and diagnostic aids have also been introduced in the treatment protocol.

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Corresponding Author:
Dr. Vijayalakshmi S,
#1893, Vasantha Colony,
Annanagar (W), Chennai-40.
E-mail: vijisigah@yahoo.com
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But the prevention of diabetes and risk modification is yet to be explored more and this has created the researchers in the field of diabetes to speculate, analyse and revise the current trends in various prevention and treatment strategies.

The scope for primordial prevention of diabetes mellitus is currently the most speculated issue in the field of diabetic research.

In this regard, various factors and variables have been taken into consideration and are under study.

It is clearly proved that though genes and familial patterns play major role in pathogenesis of diabetes mellitus, still modifiable factors like dietary patterns, life style, etc also play important role in its occurrence and pathogenesis of its complications.

So researchers are now currently doing studies taking the various dietary factors that might possibly reduce the occurrence of both incidence of diabetes and its various complications.

One such nutrient mineral which has been in the vogue of diabetic research is magnesium. Already many studies have been done and published taking into consideration the role of magnesium level in diet and occurrence of diabetes. Some studies have also been done to assess the role of magnesium levels and occurrence of diabetic complications. All of the studies have concurred with one statement that magnesium deficiency causes increased risk of developing diabetes at an early age in susceptible population. This has paved way for speculation of possible role of magnesium supplementation in prevention of diabetes mellitus and its complications. Few studies have been conducted in selected cohorts of high risk individuals and have been done as double blind trial with one group of subjects receiving magnesium supplementation while the other group acting as a placebo. Both the groups were monitored periodically and checked for diabetes status. The conclusions of these studies have proved the beneficiary effects of magnesium supplementation in delaying the occurrence of diabetes mellitus.

REVIEW OF LITERATURE: Diabetes mellitus is a group of metabolic diseases (metabolic syndrome) caused by a complex interaction of genetic, immunological and environmental factors and characterised by hyperglycaemia resulting from defects in insulin secretion, insulin action or both.[1]

It has become a pandemic disease. According to the International Diabetes Federation, diabetes affects at least 285 million people worldwide, and this number is expected to reach 438 million by the year 2030.[2] The number of adults with impaired glucose tolerance will rise from 344 million in 2010 to an estimated 472 million by 2030.[2]

Type-2 diabetes mellitus is the most common form of diabetes accounting for 90% of the cases.[3]

The prevalence of diabetes in India has increased dramatically in recent decades. The threatening effect of diabetes for these patients is chronic hyperglycaemia[2] associated with longterm damage, dysfunction and failure of various organs especially the eyes, kidneys, nerves, heart and blood vessels (ADA 2006).[1]

The Diabetes Control and Complications Trial (DCCT) demonstrated that tight control of blood glucose is effective in reducing clinical complications significantly, but even optimal control of blood glucose could not prevent complications suggesting that alternative treatment strategies are needed.[4]

One such treatment strategy under research is supplementation of magnesium and its role in primary prevention of diabetes and slowing the progression of complications related to longterm diabetes.

As an essential component of the daily diet intake, trace elements like magnesium are also important for the pathogenesis of diabetes and diabetic complications. Disturbances in trace element status and increased oxidative stress in diabetes may contribute to insulin resistance and the development of diabetes and diabetic complications.[2] On the other hand, progression of diabetes may also lead to perturbation in trace element metabolism and homeostasis.[2] Imbalances in these processes lead to high susceptibility to oxidative damage of tissues and eventually to the development of diabetes and diabetic complications.[2]

Magnesium, a mineral needed by living cells of human body,[5] is the fourth most abundant cation in the human body.[6] Magnesium is mainly seen in intracellular fluid and it is the second most abundant intracellular cation. Total body magnesium is about 25 g, 60% of which is complexed with calcium in bone.

One-third of skeletal magnesium is exchangeable with serum.

Magnesium orally produces diarrhoea; but intravenously it produces CNS depression.[7]

Mg++ is the activator of many enzymes requiring ATP. Alkaline phosphatase, hexokinase, fructokinase, phosphofructokinase, adenyl cyclase, cAMP dependent kinases, etc. need magnesium.[7] It is believed to play a role in glucose homeostasis, insulin action, and the development of type 2 diabetes.[8]

It may influence insulin secretion by interacting with cellular calcium homeostasis.[9] It was said that low serum Mg plays an important role in pathogenesis of insulin resistance. Mg can function as a mild, natural calcium antagonist. So the level of intracellular calcium is increased in Mg-deficiency subjects. This increased intracellular calcium may compromise the insulin responsiveness of adipocytes and skeletal muscles leading to the development of insulin resistance.[10]

Another study has also found that insulin deficiency or insulin resistance can affect the tubular absorption of Mg, leading to hypomagnesaemia in diabetic subjects.[11] Thus, a vicious circle is formed by mutual influence between insulin resistance and hypomagnesaemia resulting in aggravation of insulin resistance.[12]

Numerous studies demonstrated that oxidative stress, mediated mainly by hyperglycaemia-induced generation of free radicals, contributes to the development and progression of diabetes and related complications.[4] Mg has been reported to possess antioxidant property.[13]

Thus the Mg level could be low because of consumption of Mg to combat the oxidative stress associated and implicated in pathogenesis of diabetes mellitus and its longterm complications.

Magnesium intake is believed to be important in maintaining magnesium homeostasis.[5] The dietary recommendation (Recommended Dietary Allowances/RDA) for magnesium is 400 to 420 mg daily for adult men and 310 to 320 mg daily for adult women.[14] More is required during lactation.[7] However, consumption is far below this recommendation, and the high prevalence of this deficiency has been associated to several chronic diseases. Magnesium is found in most foods, but in varying concentrations. Leafy vegetables, nuts, whole grains, fruits, and legumes are

considered as foods with high-magnesium concentrations.[14]

Normal serum level Mg++ is 1.8-2.2 mg/dL. Inside the RBC, the magnesium content is 5 mEq/L. In muscle tissue, Mg++ is 20 mEq/L. About 70% of magnesium exists in free state and remaining 30% is protein-bound (25% to albumin and 5% to globulin).[7]

Homeostasis is maintained by intestinal absorption as well as by excretion by kidney.

Magnesium is reabsorbed from loop of Henle and not from proximal tubules. Insulin-dependent uptake of glucose is reduced in magnesium deficiency.[7]

Hypomagnesaemia has been shown to occur frequently among patients with diabetes, especially those with poor metabolic control.[5]

Studies in animals have shown that a diet low in magnesium leads to impaired insulin secretion and action[15] and several epidemiological studies indicate that deficient magnesium intake may be an independent risk factor for the development of type 2 diabetes mellitus.[5] Evidence suggests that magnesium supplementation could be useful in the treatment of diabetes and to prevent the development of its chronic complications.[16]

Also several studies have concluded that magnesium supplementation lowers the incidence of type 2 diabetes.[9]

The present study is taken with the objective of assessing serum magnesium level in type 2 diabetic subjects and nondiabetics and to analyse the relationship between serum magnesium level and diabetic status.

AIM OF THE STUDY: The aim of the study is to:

1. Estimate the level of serum magnesium levels in type 2 diabetic patients and controls.
2. Determination of the correlation between the level of serum magnesium in diabetics and nondiabetics.

MATERIALS AND METHODS: This study is a cross-sectional study among subjects attending the Diabetes OP, NCD OP and General OPD in Government MGM Hospital, Trichy.

All study participants provided written, informed consent and study protocol was reviewed and approved by the Institutional Ethical Committee Review Board.

Inclusion Criteria: Nondiabetics with normal blood glucose levels are taken as controls.

Those subjects who have been diagnosed to have diabetes mellitus were included in study group. i.e., patients with fasting plasma glucose (FPG) ≥ 126 mg/dL and/or 2 h plasma glucose (2 h-PG) ≥ 200 mg/dL or with a history of diabetes mellitus.

Exclusion Criteria:

- Malabsorption syndrome.
- Diuretic therapy.
- Hyperparathyroidism.
- Uraemia.
- Chronic renal failure.
- Glomerulonephritis.
- Intensive antacid therapy.

Study Protocol: The subjects were included based on the information got by a standard interview questionnaire. The questionnaire included their demographic characteristics, lifestyle, the history of chronic diseases, and current use of medication, including antidiabetic drugs, smoking and alcohol intake, etc. Blood pressure was measured and body height, weight were recorded. Complete general examination was done.

METHOD: After at least 10 hours of overnight fasting, venous blood samples of all participants was collected for the measurements of blood glucose, BUN, serum creatinine, lipid profile and serum magnesium. (Serum must be separated from the clot as soon as possible or the level of magnesium will increase because of its elution from the red blood cells. Haemolysed samples as well as blood collected with citrate, oxalate or EDTA are unacceptable for analysis).

Blood glucose was measured with the use of the glucose oxidase method on a semi-auto analyser.

BUN was assayed using UV kinetic method using a semi-auto analyser.

Serum creatinine was estimated by the Jaffe's kinetic method using semi-auto analyser.

Triglycerides (TG), total cholesterol (TC) and high-density lipoprotein cholesterol (HDLc) were measured by enzymatic methods using a semi-auto analyser. Low-density cholesterol (LDLc) was calculated using Friedwald's formula. Serum magnesium was assayed using endpoint photometric method with Xylidyl blue reagent using a fully automated bench top analyser.

RESULTS AND STATISTICS: The total number of subjects included for the study was 100. Out of this, 50 were in control group and remaining 50 were in study group.

It is an age and sex matched study. The baseline demographic characteristics and results of variables done in this study are given below:

	Controls (n=50)	**Type 2 Diabetics n=50**
Age (yrs.) (mean) (std. dev.)	56.92 9.59	59.6 8.16
Sex males	31	29
Females	19	21
BP-systolic (mean)(mmHg)	146	148
BP-diastolic (mean)(mmHg)	82	94
Smoking	13	17
Alcohol status	9	15
Blood urea nitrogen(mg/dL) Mean Std dev	 19.36 2.4	 18.63 1.74

Serum creatinine(mg/dL) Mean Std dev	1.07 0.22	1 0.14
Fasting blood glucose(mean) Mg/dl (std dev)	91.8 16.8	145.8 23.4
Total cholesterol(mean) Mg/dl (std dev)	164 13.39	262 11.30
Triglycerides(mean) (mg/dl) (std dev)	120 9.21	174 7.87

Table 1

The magnesium levels in control and diabetic subjects were statistically analysed using student unpaired t test. The results of data and statistical significance are given below:

	Control	**Diabetics**	t value for the data is 7.589-e13
Number(n)	50	50	
Magnesium level- Mean value Std dev	2.6 0.37	1.1 0.38	p value is < 0.001 statistically significant

Table 2

DISCUSSION: In our study the diabetic group of subjects show a significantly lower level of serum magnesium as compared to the control subjects. The mean magnesium level in Diabetic group is 1.1 mg/dl while it is 2.6 mg/dl in the control group. This difference was analysed using standard statistical tool and found to be not due to chance alone. The student's t test was used and the t value got corresponds to a p value of <0.001 which is very significant. This is concordant with the conclusions of other workers.[16,17,18] A. R. Srinivas et al in his paper has concluded that serum magnesium levels and triglycerides are both significantly and independently associated with Diabetes Mellitus, the former being negatively correlated and latter being positively correlated.[18]

In one study, Wang et al., says that the various ions in serum are significantly affected in Diabetic population in China.[19] Cellular magnesium deficiency can significantly alter the sodium-potassium ATPase which is involved in maintenance of gradients of sodium, potassium and glucose across membranes.[20] Also, it affects the secretion of insulin from pancreas. Put together Magnesium deficiency will adversely affect the glucose homeostasis and may contribute in the pathogenesis of Diabetes Mellitus.

Also, the patients with diabetes may go in for hypomagnesaemia by some unknown mechanisms. One possibility is that the hyperglycaemia and glucosuria seen in diabetic subjects may osmotically lead to increased magnesium loss in urine leading to hypomagnesaemia and the resultant hypomagnesaemia may in turn worsen the diabetic status by altering insulin secretion further. Thus, it is a two-way process.

And moreover many studies have also concluded the beneficiary role of magnesium supplementation in diabetic subjects. One such study published in the Journal Of Clinical Nutrition, done by Cristiane Hermes Sales et al., has concluded the beneficiary role of magnesium supplementation in glucose control in selected subjects with type 2 diabetes mellitus.[21]

Thus, clearly magnesium ion has a significant role in both causal mechanisms, progression and onset of complications and the dietary supplementation of magnesium can improve outcome and decrease the morbidity and mortality associated with the disease spectrum.

CONCLUSION: From the analysis of data, the following conclusion is made:

1. The serum magnesium level is lowered in diabetes mellitus and this lowering cannot be due to chance alone. i.e., there is significant correlation between low serum magnesium level and diabetes mellitus.

LIMITATIONS OF OUR PRESENT STUDY: Sample size does not reflect the true incidence and prevalence of the disease.

Other confounding variables like dietary patterns between subject groups were not taken into consideration.

FUTURE SCOPE OF THE STUDY: The next study can be done as a cohort study choosing high risk subjects who are nondiabetic grouped according to their existing serum levels of magnesium into those with low magnesium levels and those with high magnesium levels and then doing a close watch on both the groups with periodical workups looking for the onset of diabetes mellitus. In this way, we can prove the causal role of decreased magnesium level in pathogenesis of diabetes in high risk groups.

Also, we can conduct a RCT (double blind trial) to know the significance of magnesium supplementation in prevention/postponement of complications in diabetes mellitus.

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