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Original Article

Study of Association of Serum Magnesium with Diabetes Mellitus at a Tertiary Care Teaching Centre

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ABSTRACT

Objective: The association between diabetes mellitus and hypomagnesaemia is compelling for its wide ranging impact on diabetic control and complications Present study was conducted to evaluate the relationship between serum magnesium levels and diabetes mellitus.

Material and Methods: The study was carried out on 25 age and sex matched healthy controls and 50 type 2 diabetic patients. Serum magnesium levels were estimated by Calmagite dye method.

Results: Statistically significant low values of serum magnesium were obtained (P<0.001) in patients of diabetes without complications when compared with controls. Further significant low values of serum mg (P<0.001) were found in patients of DM with complications when compared with DM without complications and controls.

Conclusion: Magnesium is an essential ion involved in multiple levels in insulin's secretion, its binding and its activity; and it is also a critical cofactor of many enzymes in carbohydrate metabolism. Serum magnesium levels are helpful to monitor the severity of complications in type 2 diabetes and also be useful for proper medical intervention to reduce complications due to diabetes.

KEYWORDS: Type-2 diabetes, Hypomagnesaemia, Complications.

INTRODUCTION

Glaser and Halpern in 1929 noticed that yeast extracts potentiate the action of insulin. Since then speculation regarding the role of bodily trace elements in human disease has gained attention.[1] Mertz, *et al.* in 1959 demonstrated the existence of glucose tolerance factor in yeast with the identification of the active component as trivalent chromium.[2] Direct associations of trace macro elements with Diabetes mellitus have been observed in many research studies.[3]

Magnesium (Mg), is the fourth most common cation in the body, with an essential role in fundamental biological reactions, whose deficiency provokes biochemical and symptomatic alterations in the human organism.[4,5] This ion is now established as a central electrolyte in a large number of cellular metabolic reactions, including DNA and protein synthesis, neurotransmission, and hormone receptor binding. It is a component of GTPase and a cofactor for Na+/ K +-ATPase, adenylate cyclase, and phosphofructokinase. Magnesium is a cofactor in more than 300 cellular enzymatic systems and has a key role in cellular metabolism; the recognition that Mg deficiency or excess may be associated with significant clinical consequences has resulted in an increased interest in the utility of serum Mg measurement.[6]

Diabetes mellitus (DM), characterized by metabolic disorders related to high levels of serum glucose, is probably the most associated disease to Mg depletion in intra and extra cellular compartments.[7,8] In several studies reduced magnesium concentrations have been observed in diabetic adults.[9-12] Hypomagnesemia has been related as a cause of insulin resistance, also being a consequence of hyperglycemia, and when it is chronic leads to the installation of macro and microvascular complications of diabetes, worsening the deficiency of Mg.[13-15]

The association between diabetes mellitus and hypomagnesaemia is compelling for its wide ranging impact on diabetic control and complications. Magnesium depletion has been linked to the development of diabetic complications like retinopathy. Hypomagnesaemia has been linked to poor glycemic control, coronary artery diseases, hypertension, and diabetic neuropathy and foot ulcerations. The etiology of

hypomagnesiamea cannot be clearly explained and serum magnesium levels have been shown to be inversely related to the severity of diabetes.[16-18]

Present study was conducted to evaluate the relationship between serum magnesium levels and diabetes mellitus.

MATERIAL AND METHODS

The present study was carried out in the Department of Biochemistry, Rajshree Institute of Medical Sciences & Research centre, Bareilly, UP, India.

The study was carried out on 25 age and sex matched healthy controls and 50 type 2 diabetic patients who attended the outpatient and inpatient department of Rajshree Institute of Medical Sciences & Research centre, Bareilly, UP (India). A total 50 patients of type 2 diabetes mellitus between 30–75 years, which were divided into following groups.

Group I: Included 25 patients of type 2 diabetes without complications.

Group II: Included 25 patients of type 2 diabetes with proven complications, like CAD, retinopathy and neuropathy.

Control group: Included 30 healthy, age and sex matched individuals.

Inclusion Criteria

Patients in the age group of 30–75 years with type 2 diabetes without and with proven complications, like CAD, neuropathy and retinopathy were selected.

Exclusion Criteria

Patients with recent infectious disease, immunological disorders, taking diuretics and magnesium containing antacids, malabsorption syndrome, chronic diarrhea, renal failure, pancreatitis, alcoholism, liver diseases, tuberculosis, thyrotoxicosis, any malignancy, any other chronic disease were excluded from the study.

Informed consent was taken from all subjects. Baseline demographic and clinical data including age and sex, detailed medical history including conventional risk factors, clinical examinations and relevant investigations including ECG, echocardiogram, nerve conduction test, fundoscopy etc were included as part of the methodology.

Serum magnesium levels were estimated by Calmagite dye method.[19] PPBS were estimated 2 hours after breakfast. Urine sample was analyzed for protein and sugar.

Student `t' test /Chi-square test has been used to find the significance of homogeneity of study characteristics between three groups of patients. Analysis of variance has been used to find the significance of study parameters between three groups. Results were expressed as mean $\pm$ SD. Probability values of $P< 0.05$ were considered to indicate statistical significance

RESULTS

Statistically significant low values of serum magnesium were obtained ($P<0.001$) in patients of diabetes without complications when compared with controls. Further significant low values of serum mg ($P<0.001$) were found in patients of DM with complications when compared with DM without complications and controls. (Table 1)

Table 1: Serum Magnesium levels in the present study.

Study parameter	Controls	DM without complications	DM with Complications
Serum Mg Mean±SD	1.98±0.43	1.53±0.49**	1.22±0.47**

P < 0.001 highly significant

DISCUSSION

Many trace elements are important for human metabolic function. Numerous studies have demonstrated the essential roles of trace elements as chromium, zinc, magnesium, selenium, vanadium, molybdenum and margenase in insulin action and carbohydrate metabolism. The actual role of these trace elements in the pathogenesis and progress of diabetes is still unclear. The observed alterations in the status of these elements in diabetics have been attributed to hyperglycemia and increased protein glycosylation.[20-22]

Magnesium is a cofactor in the glucose transporting mechanisms of the cell membrane and various enzymes in carbohydrate oxidation. It is also involved at multiple levels in insulin secretion, binding and enhancing the ability of insulin to activate tyrosine kinase. Magnesium deficiencies have been implicated in insulin resistance, carbohydrate intolerance, dyslipidemia and complications of diabetes.[23,24]

In present study, we observed that the mean serum magnesium level was statistically significantly low ($P<0.001$) in Diabetic patients with and without complications when compared with controls. This indicates the association of reduced serum magnesium levels with diabetes. In our study, serum magnesium level in cases with diabetic complications (1.22±0.47) was much lower than those without complications (1.53±0.49). Similar results were obtained by few researchers in past.[13,25-27] Aradhana Sharma et al and Diwan, et al. reported that serum magnesium levels were significantly lowered in patients with diabetic complications when compared to diabetic patients

without complications.[28,29] Ishrath Kareem et al found that serum magnesium levels in patients with diabetic retinopathy were significantly lowered compared to patients without retinopathy.[30]

Lefebvre P J, Scheen A J stated that insulin secreted by a glucose challenge is partly dependent on adequate magnesium. Insulin, via its interaction with ligand activated tyrosine protein kinase associated receptors, initiates a cascade of biochemical interactions that result in several physiological, biochemical and molecular events that are involved in carbohydrate, lipid and protein metabolism.[31] The ability of insulin once bound to receptor to activate tyrosine kinase is reduced in hypomagnesaemia states; as a result reduced peripheral glucose uptake and oxidation are often noted in subjects with hypomagnesaemia. Decrements in the enzymatic activities of several metabolic pathways are seen in DM patients as a result of the relative magnesium deficiency.[23,32]

Despite numerous reports linking hypomagnesaemia to chronic diabetic complications, attention to this issue is poor among clinicians. The precise mechanism for development of microvascular changes is not fully understood, it is possible that hypomagnesaemia inhibits prostacyclin receptor function producing an imbalance between prostacyclin and thromboxane effect which has marked atherogenic potential which is responsible for microvascular complications.[27]

Magnesium is an essential ion involved in multiple levels in insulin's secretion, its binding and its activity; and it is also a critical cofactor of many enzymes in carbohydrate metabolism. Serum magnesium levels are helpful to monitor the severity of complications in type 2 diabetes and also be useful for proper medical intervention to reduce complications due to diabetes.

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