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## Can Magnesium be an Influencing Element in Type 2 Diabetics?.

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### ABSTRACT

Magnesium plays an important role in carbohydrate metabolism. It serves as a co-factor for all enzymatic reactions that require ATP and as a key component in various reactions that require kinases. It may influence the release and activity of insulin. Low blood levels of magnesium are frequently seen in individuals with type 2 diabetes. The kidneys possibly lose their ability to retain magnesium during periods of severe hyperglycemia resulting in lower magnesium levels. Insulin resistance and magnesium depletion result in a vicious cycle of worsening insulin resistance and decrease in intracellular magnesium which limits the role of magnesium in vital cellular processes. Glycated haemoglobin and serum magnesium were estimated in 50 previously diagnosed cases of diabetes type 2 from diabetic clinic at PGIMS, Rohtak and 50 age and sex matched healthy individuals with normal blood sugar were taken as control. Serum magnesium was found to be significantly lower in diabetics ( $p < .001$ ) than controls but within normal reference range (1.77 mg/dl). In diabetic group, serum magnesium depicted significant negative relation with HbA1c and duration of the disease ( $r^2 = 0.72$ ,  $p = 0.013$ ). Patients with diabetes have significant lower magnesium and thus might be at increased risk of magnesium related complications. Periodic determination of magnesium levels and intake of magnesium rich foods and magnesium supplements is recommended in type 2 diabetics to avoid the complications.

**Keywords-** Magnesium, Insulin resistance, Glycated haemoglobin, Diabetes

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## INTRODUCTION

Magnesium (Mg) is an important intracellular cation that is distributed into three major compartments: mineral phase of bones (65%), intracellular space (34%) and extracellular fluid (1%) [1]. It is needed for more than 300 biochemical reactions in the body and serves as a co-factor for all enzymatic reactions that require ATP and as a key component in various reactions that require kinases. It is also an essential enzyme activator for neuromuscular excitability and cell permeability, a regulator of ion channel and mitochondrial function, a critical element in cellular proliferation and apoptosis, and an important factor in both cellular and humoral immune reactions [2].

Type-2 diabetes is characterized by insulin resistance and usually relative insulin deficiency. Most of these patients are obese and at increased risk of developing macrovascular complications. In these patients insulin secretion is defective and insufficient to compensate for the insulin resistance [3].

Magnesium plays an important role in carbohydrate metabolism. It may influence the release and activity of insulin, the hormone that helps to control blood glucose levels [4]. Low blood levels of magnesium are frequently seen in individuals with type-2 diabetes. Hypomagnesaemia may worsen insulin resistance. The kidneys possibly lose their ability to retain magnesium during periods of severe hyperglycemia. The increased loss of magnesium in urine may then result in lower blood levels of magnesium [5]. Insulin resistance and magnesium depletion result in a vicious cycle of worsening insulin resistance and decrease in intracellular  $Mg^{2+}$  which limits the role of magnesium in vital cellular processes [6]. So present study has been designed to study serum magnesium levels in diabetics.

## MATERIALS AND METHODS

The present study was conducted at the Department of Biochemistry, PGIMS, Rohtak. Fifty type-2 DM patients within age group of 30-75 years attending the Diabetic OPD PGIMS, Rohtak were included in this study. Type-2 DM patients were diagnosed on the basis biochemical investigations as per WHO criteria [3].

Fifty age and sex matched apparently healthy individuals with normal plasma glucose & with no symptoms suggestive of DM were taken as controls. Patients with acute & chronic inflammatory conditions, other metabolic conditions like ketoacidosis, cerebrovascular disease or renal diseases as well as smokers, alcoholics, and primary hypertensive were excluded from the study. All the diabetics were under treatment with oral hypoglycaemic agent or insulin - Insulin crystal injections with various dosages.

Specific tests for serum Magnesium was done by collecting the blood in plain red capped plastic tube. Magnesium was estimated by xylydyle blue dye method by autoanalyser [7]. The reference serum or plasma magnesium level by this method is 1.7-2.7 mg/dl. The principle of this method is that magnesium ion reacts with xylydyle blue in an alkaline medium to form a water soluble purple red chelate. Chelating agent and detergent present in the reagent will help out interference occurring from Calcium and Proteins. The intensity of the purple colour is proportional to magnesium concentration.

Correlation between HbA1c and serum magnesium of diabetics and between serum magnesium of cases and control was depicted by SPSS software.

### RESULTS AND DISCUSSION

In diabetic group serum magnesium depicted significant negative relation with HbA1c ( $r^2 = 0.72$ ,  $p < 0.001$ ) (Figure 1). Also, serum magnesium was found to be significantly lower in diabetics ( $p = .013$ ) than controls but within normal reference range (1.77 mg/dl) (Table-1).

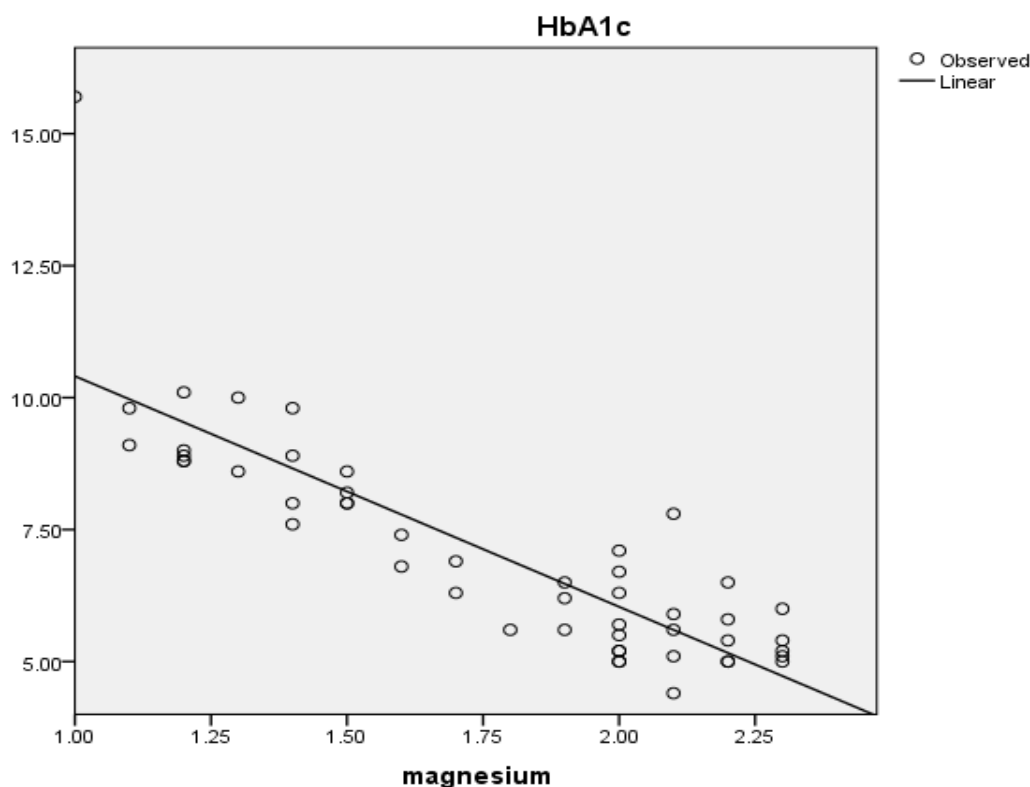


Figure 1- Correlation between HbA1c and serum magnesium of diabetics

Table 1- Comparison of serum magnesium level of diabetics and controls

Group	N	Mean Magnesium level	Std. Deviation	Std. Error Mean
Diabetics	50	1.7700	0.40064	0.05666
Controls	50	2.2060	0.33284	0.04707

The principal finding of the present study was a significant inverse correlation of serum Mg in DM with normal controls. We also got a significant negative correlation of serum Mg with HbA1c in diabetic patients.

Magnesium is a cofactor for several enzymes involved in carbohydrate metabolism. There is a strong relationship between magnesium and insulin action. The magnesium homeostasis is tightly regulated and depends on the balance between intestinal absorption and renal excretion [8]. Reduced serum magnesium may result from enhanced renal magnesium excretion. As insulin has been related to magnesium reabsorption at the thick ascending limb of the loop of Henle, insulin deficiency or resistance can promote magnesium wasting at this nephron segment [8,2]. In addition, hyperglycemia and

glycosuria may also interfere with renal magnesium handling, mainly by reducing the tubular reabsorption of the cation [10]. Other potential causes of lower serum magnesium in obese type 2 diabetic patients include reduced intestinal magnesium absorption secondary to higher fat intake and lower fibre intake [11,12]. As insulin enhances the transport of magnesium into cells, lack of insulin may result in an intracellular magnesium deficit [13,14]. In states of insulin resistance, insulin induced cellular entry of magnesium is impaired [15]. A recent study showed that pioglitazone, an insulin sensitizer, increases free magnesium concentration in insulin-responsive tissues such as adipocytes [16]. Reduced intracellular magnesium concentrations result in an altered cellular glucose transport, a defective phosphorylation of tyrosine-kinase, post-receptor impairment in insulin action by influencing intracellular signalling and processing, and reduced pancreatic insulin secretion [8,17]. In addition, chronic magnesium deficiency has also been associated with elevated concentrations of TNF-alpha, which also contribute to post-receptor insulin resistance [18]. Therefore, T2DM could facilitate low serum magnesium levels and this could in turn worsen glycemic control of diabetes, thus establishing a vicious circle that could lead to a progressive impairment in metabolic control and more risk of diabetic complications.

According to American Diabetes Association, serum magnesium levels should be measured in diabetes patients at high risk for magnesium deficiency who have diabetes with concomitant conditions like acute myocardial infarction, calcium deficiency, congestive heart failure, ethanol abuse, ketoacidosis, long-term parenteral nutrition, long-term use of certain drugs (such as diuretics, digoxin or aminoglycosides), potassium deficiency and pregnancy [19].

Deficiency of magnesium is also closely linked to abnormalities in calcium and potassium metabolism. A fundamental interaction between magnesium and other ions seems to occur at the cellular level [20]. Hypomagnesaemia can increase platelet reactivity, increase vascular and adrenal responses to angiotensin II, enhance thromboxane A2 (TXA2) release, and lead to organ damage from free radicals [21,22]. It may be a contributing factor to complications like ischemic heart disease [23], retinopathy [24,25] and bone loss [26].

In several studies, daily oral magnesium supplementation substantially improved insulin sensitivity by 10% and reduced blood sugar by 37% [27,28].

## CONCLUSION

Patients with diabetes have significant lower magnesium and thus might be at increased risk of complications related to magnesium. We recommend periodic determination of magnesium levels and intake of magnesium rich foods like whole grains, legumes, fruits and vegetables (especially dark-green, leafy vegetables) every day which will help to provide recommended intakes of magnesium and maintain normal storage levels of this mineral. Dietary intake of magnesium can often restore mildly depleted magnesium levels but magnesium supplementation is required to restore very low magnesium levels to normal. To examine the effect of magnesium replacement on outcomes, a long-term prospective study is needed.

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