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A study on estimation of fasting serum magnesium levels in type 2 diabetes mellitus

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Abstract

Magnesium deficiency is proposed as a factor in the pathogenesis of diabetic complications. Hypomagnesemia can be both a cause and a consequence of diabetic complications. The aim of our study was to know the relationship between magnesium levels and diabetes, association with level of control of diabetes and magnesium levels in relation to complications of diabetes. A cross sectional study done with 150 patients with Type 2 Diabetes mellitus in outpatient and inpatient departments in Medicine, to estimate the levels of fasting serum magnesium levels in Type 2 Diabetics. To correlate the magnesium levels with the Diabetic Complications. Among the microvascular complications, retinopathy was found in 35.6% of cases, nephropathy in 20% of cases and neuropathy in 11% Hypomagnesemia was found in 78.1% of retinopathy, 55.6% of nephropathy and 30% of neuropathy cases. Among the macrovascular complications, IHD was found in 22.2%, CVA was found in 6.7% and PVD in 4.4%. Hypomagnesemia was found in 60% of cases of IHD, 50% of cases of CVA and PVD. Serum magnesium levels were low in type 2 diabetics when associated with complications. Hypomagnesemia was associated with diabetic retinopathy, diabetic nephropathy and Ischemic Heart Disease.

Keywords: Type 2 diabetes mellitus, low magnesium levels

Introduction

Diabetes mellitus (DM) refers to a group of common metabolic disorders that share the phenotype of hyperglycemia. Several distinct type of DM is caused by a complex interaction of genetics and environmental factors. Depending upon the etiology of the DM, factors contributing to hyperglycemia include reduced insulin secretion, decreased glucose utilization, and increased glucose production. The metabolic dysregulation associated with DM causes secondary pathophysiologic changes in multiple organ systems, leading to microvascular (retinopathy, nephropathy, neuropathy) and macrovascular (coronary heart disease, peripheral arterial disease, cerebrovascular disease) [1].

Low magnesium status has repeatedly been demonstrated in patients with type 2 diabetes. Magnesium deficiency appears to have a negative impact on glucose homeostasis and insulin sensitivity in patients with type 2 diabetes [2]. Magnesium deficiency has been found to be

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associated with microvascular disease in diabetes. Hypomagnesemia has been demonstrated in patients with diabetic retinopathy, lower levels of magnesium predicting a greater risk for diabetic retinopathy. Magnesium depletion has also been associated with arrhythmogenesis, vasospasm, platelet activity and hypertension.

25 to 39% of outpatient diabetics have low concentrations of serum magnesium and numerous studies have shown 4 lower serum magnesium concentrations in type 2 diabetics compared to healthy controls.

The reasons why magnesium deficiency occurs in diabetes are not clear, but may include increased urinary loss, lower dietary intake, or impaired absorption of magnesium compared to healthy individuals [3].

Several studies have reported increased urinary magnesium excretion in type 1 and 2 diabetes, some reporting a correlation between glycemic control and urinary magnesium loss.

Magnesium is involved in insulin secretion, binding and activity. Cellular deficiency of magnesium can alter the membrane bound sodium-potassium-adenosine triphosphatase which is involved in maintaining the gradient of sodium and potassium and also in glucose transport.

Low dietary intake may also contribute to low magnesium status in diabetics. Patients with type 2 diabetes are often overweight, and may consume a diet higher in fat and lower in magnesium density than non-diabetics. However, the few studies that have reported magnesium intake in type 2 diabetes are equivocal [4].

Impaired intestinal absorption might also contribute to low magnesium status in diabetics. However, there are no published data on magnesium absorption in humans with diabetes. Despite the growing realization of the importance of magnesium in human health and disease, measurement of magnesium status remains problematic. Serum magnesium concentrations can be normal despite depletion of intracellular magnesium [5].

Mg deficiency may result in disorders of tyrosine-kinase activity on the insulin receptor, event related to the development of post-receptorial insulin resistance and decreased cellular glucose utilization16 that is, the lower the basal Mg, the greater the amount of insulin required to metabolize the same glucose load, indicating decreased insulin sensitivity [6].

Methodology

Source of data

- Patients with Type 2 Diabetes mellitus in outpatient and inpatient departments in Medicine.

Method of collection of data

- **Sample size:** 150.
- **Type of study:** Cross sectional.

150 patients with Type 2 DM underwent the following tests

1. Detailed history.
2. Clinical Examination.
3. Glycemic Status (FBS, PPBS, HbA1C).
4. Fasting Serum Magnesium Levels.
   Method: Colorimetric method using calmagite dye.
   Reference range: 1.8-2.5 mg/dL.
5. Fundoscopy.
6. Urinary analysis.

ISSN 2515-8260 Volume 09, Issue 02, 2022

7. Blood urea & serum creatinine.
8. Monaofilament test.
9. ECG.

Inclusion criteria

- Age > 18 yrs.
- Diagnosed cases of Type 2 Diabetes Mellitus based on FBS, PPBS.

Exclusion criteria

- Alcohol abuse.
- Patients on loop or thiazide diuretics.
- Patients on antibiotics like Aminoglycosides.
- Pregnancy.
- Congestive heart failure.
- Long term parenteral nutrition.

Estimation of serum magnesium

Colorimetric method using calmagite dye:

Test principle

Under alkaline conditions, magnesium ions react with calmagite to produce a red complex which is measured spectrometrically at 530 nm. The intensity of the color produced is directly proportional to the concentration of magnesium in serum.
EGTA is included in the reagent to estimate the interference of calcium during estimation. Heavy metal interference is prevented by the presence of cyanide and a surfactant system to remove protein interference.

Results

Table 1: Microvascular and macrovascular complications

No. of cases with only microvascular complications	No. of cases with only Macrovascular complications	No. of cases with both microvascular & macrovascular complications
60	30	45
66.7%	33.3%	50%

Out of 90 cases of type 2 DM who had complications; 60 subjects had only microvascular complications (45%), 30 subjects had only macrovascular complications (22%) and 45 subjects had both microvascular & macrovascular complications (33%).

Table 2: Hypomagnesemia & Complications

No of cases with complications	Hypomagnesemia	Normomagnesemia
90	55	35
	61.1%	38.8%

Out of 90 cases of Type 2 DM who had complications; 55 subjects turned out to have hypomagnesemia (61%) and 35 subjects (39%) had normal serum magnesium levels.

ISSN 2515-8260 Volume 09, Issue 02, 2022

Table 3: Microvascular complications

Complication	No. of cases	With low Mg	With normal Mg	Percent of cases with low Mg
Retinopathy	32	25	7	78.1%
Nephropathy	18	10	8	55.6%
Neuropathy	10	3	8	30%

Retinopathy was found in 32 subjects of which 25 had hypomagnesemia (78.1%).
Nephropathy was found in 18 subjects of which 10 had hypomagnesemia (55.6%).
Neuropathy was found in 10 subjects of which 3 had hypomagnesemia (30%).

Table 4: Macrovascular complications

Complication	No. of cases	With low Mg	With normal Mg	Percent of cases with low Mg
IHD	20	12	8	60%
CVA	6	3	3	50%
PVD	4	2	2	50%

Ischemic heart disease was found in 20 subjects of which 12 had hypomagnesemia (60%).
Cerebrovascular accident was found in 6 subjects of which 3 had hypomagnesemia (50%).
Peripheral vascular disease was found in 6 subjects of which 3 had hypomagnesemia (50%).

Discussion

61.1% of complications were associated with hypomagnesemia. Among the microvascular complications, retinopathy was found in 35.6% of cases, nephropathy in 20% of cases and neuropathy in 11% Hypomagnesemia was found in 78.1% of retinopathy, 55.6% of nephropathy and 30% of neuropathy cases. Among the macrovascular complications, IHD was found in 22.2%, CVA was found in 6.7% and PVD in 4.4%. Hypomagnesemia was found in 60% of cases of IHD, 50% of cases of CVA and PVD.

Our study results are similar to *Valk HW et al*., which showed that patients with diabetic retinopathy present low concentration of plasma magnesium levels, disposing to a higher risk of advanced retinopathy [7].

Our study results are also similar with *Arundathi dasgupta et al*. where Retinopathy, microalbuminuria, macroalbuminuria, foot ulceration, and neuropathy was present in 64%, 47%, 17.64%, 58.8%, and 82.35%, respectively, of the patients with hypomagnesemia as compared with 45.8% [8].

Another study Fujii *et al*., results were similar, where retinopathy was associated with marked depletion in plasma and erythrocyte magnesium levels in diabetic patients [9].

Hypomagnesemia occurs at an incidence of 13.5 to 47.7% among patients with type 2 diabetes. Poor dietary intake, autonomic dysfunction, altered insulin metabolism, glomerular hyperfiltration, osmotic diuresis, recurrent metabolic acidosis, hypophosphatemia, and hypokalemia may be contributory. Hypomagnesemia has been linked to poor glycemic control, coronary artery diseases, hypertension, diabetic retinopathy, nephropathy, neuropathy, and foot ulcerations. The increased incidence of hypomagnesemia among patients with type 2 diabetes presumably is multifactorial. The correction of low serum Mg levels has never been proved to be protective against chronic diabetic complications, intervention is justified because hypomagnesemia has been linked to many adverse clinical outcomes. In addition, Mg supplementation is inexpensive and a relatively benign medication. Nonetheless, close observation must be given to those with renal insufficiency [10].

Hypomagnesemia has been reported in patients with diabetic retinopathy. With lower serum magnesium levels predicting a greater risk of severe diabetic retinopathy. 65 The present

study revealed a definite association between diabetic retinopathy and low serum magnesium levels. The mechanism by which hypomagnesemia predisposes to retinopathy is not clear.
Grfton *et al*. [11] have proposed the inositol transport theory to explain this association. But the exact reason remains obscure.
In a study done by Ishrat Kareem *et al*. [12] found that patients with diabetic retinopathy showed significant rise in serum cholesterol and triglyceride. So they stated that probably hypomagnesemia and increased serum cholesterol and triglyceride levels are responsible for microvascular changes in diabetes leading to retinopathy. There was no association seen with magnesium levels in patients with neuropathy.

Conclusion

Serum magnesium levels were low in type 2 diabetics when associated with complications Hypomagnesemia was associated with diabetic retinopathy, diabetic nephropathy and Ischemic Heart Disease. No correlation was found in respect to Neuropathy, peripheral vascular disease and Cerebrovascular Accident. Hypomagnesemia is a factor in type 2 diabetes and associated with various complications and duration of diabetes leading to various complications.

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