



A STUDY OF RELATIONSHIP BETWEEN SERUM MAGNESIUM AND COMPLICATIONS OF DIABETES IN TYPE 2 DIABETES MELLITUS PATIENTS

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ABSTRACT

Introduction: Diabetes mellitus (DM) refers to a group of common metabolic disorders that share the phenotype of hyperglycemia. It results from defects in insulin secretion, insulin action or both. Diabetes mellitus impairs the metabolism of carbohydrates, proteins, fats, water and electrolytes. These metabolic disturbances lead to permanent and irreversible functional and structural changes in the body which in turn leads to the development of “diabetic complications” affecting, the cardiovascular system, nervous system, renal system and eyes. Diabetes has shown to be associated with abnormalities in the metabolism of any micronutrients. Out of these magnesium has been investigated as a clinically significant electrolyte. Magnesium depletion has a negative impact on glucose homeostasis and insulin sensitivity in patients with type 2 diabetes as well as on the evolution of complications such as retinopathy, arterial atherosclerosis and nephropathy. Hypomagnesemia occurs with an increased frequency among patients with type 2 diabetes as compared with non diabetes according to the previous studies. Hence, this study was undertaken to find the relationship between serum magnesium and diabetic retinopathy, nephropathy and foot ulcers in type 2 diabetes mellitus patients. **Materials & Methods:** It is an observational study done on 100 patients with diabetic retinopathy, diabetic nephropathy, and diabetic foot ulcer. **Results:** The serum magnesium levels were low (<1.5 mg/dL) in 72% of the diabetics. The mean serum magnesium levels were 1.32±0.27 mg/dL. **Conclusion:** In our case study, it was concluded that there is a strong relationship between hypomagnesemia and diabetic complications that is diabetic retinopathy, nephropathy and diabetic foot ulcer.

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INTRODUCTION

Diabetes mellitus (DM) refers to a group of common metabolic disorders that share the phenotype of hyperglycemia. It results from defects in insulin secretion, insulin action or both.[1] Type 2 diabetes comprises the majority of people with diabetes around the world, and is largely due to the result of excess body weight and physical inactivity.[1] International Diabetes Federation (IDF) estimates the total number of diabetic subjects to be around 40.9 million in India and this is further set to 69.9 million by the year 2025.[2] Diabetes mellitus impairs the metabolism of carbohydrates, proteins, fats, water and electrolytes. These metabolic disturbances lead to permanent and irreversible functional and structural changes in the body which in turn leads to the development of “diabetic complications” affecting, the cardiovascular system, nervous system, renal system and eyes.[3] Complication of diabetes mellitus can be divided into vascular and nonvascular complications.

The vascular complications of DM are further subdivided into microvascular (retinopathy, neuropathy, nephropathy) and macrovascular complications (coronary artery disease (CAD), peripheral arterial disease (PAD), cerebrovascular disease).[1] Adults with diabetes have increased risk of heart attacks and strokes.[4] Due to reduced blood flow and neuropathy the chances of foot ulcers increases and eventually the need for limb amputation can occur.[5] diabetes has shown to be associated with abnormalities in the metabolism of many micronutrients.[6] Out of these magnesium has been investigated as a clinically significant electrolyte.[7] Studies have shown that magnesium levels are lower in patients with diabetes compared with nondiabetic controls.[8] The reported incidence of hypomagnesemia in patients with type 2 DM varies between 13.5 to as high as 47.7%.[9] Magnesium depletion has a negative impact on glucose homeostasis and insulin sensitivity in patients with type 2 diabetes as well as on the evolution of complications such as retinopathy, arterial atherosclerosis and nephropathy. Hypomagnesemia occurs with an increased frequency among patients with type 2 diabetes as compared with non diabetes according to the previous studies. Despite numerous reports linking hypomagnesemia to chronic diabetic complications, attention to this issue is poor among

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clinicians. Further, hypomagnesemia very often remains under-diagnosed and under-evaluated due to its usual asymptomatic presentation. Also, to date, there are very few studies which have shown the association of serum magnesium levels with diabetic complications especially in India. Hence, this study was undertaken to find the relationship between serum magnesium and diabetic retinopathy, nephropathy and foot ulcers in type 2 diabetes mellitus patients.

MATERIALS AND METHODS

The present study was an observational study entitled “A study of relationship between serum magnesium and complications of diabetes in type 2 diabetes mellitus patients” was conducted at Sri Aurobindo Medical College & PG Institute, Indore, a 1200 bedded a tertiary care and referral center situated in heart of the city with state of the art technology catering to all sections of the society.

Duration of Study

The study was conducted from December 2015 to June 2017 among the patients who were admitted at Sri Aurobindo Medical College & PG Institute, Indore.

Sample Size

100 patients with diabetic retinopathy, diabetic nephropathy, and diabetic foot ulcer were enrolled for the study.

Inclusion Criteria

1. Patients with Type 2 diabetes mellitus who are taking Oral Hypoglycemic drugs (OHA) and /or insulin.
2. Patients with diabetic retinopathy, diabetic nephropathy and foot ulcers

Exclusion Criteria

1. Patients receiving magnesium supplements or magnesium containing antacids.
2. Patients with chronic diarrhea or malabsorption.
3. Procedure Planned:- All relevant Blood Investigations, Fundus examination

OBSERVATIONS AND RESULTS

The data was analysed and the final results and observations were tabulated and interpreted as below

Table 1 Distribution of study population according to the age

Age group (Years)	Distribution (n=100)	
	Number	Percentage
31 to 40	7	7.00
41 to 50	28	28.00
51 to 60	41	41.00
61 to 70	21	21.00
71 to 80	3	3.00
Total	100	100.00

In this study 41% of the patients were aged between 51 to 60 years. The mean age was 55.26±9.32 years and median age was 55 years with range 35 being minimum and 80 being maximum.

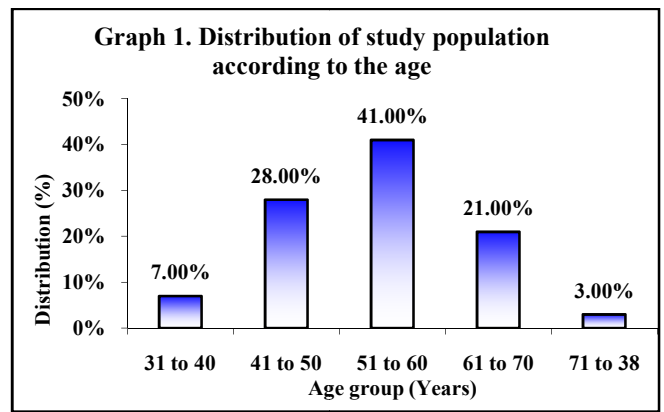
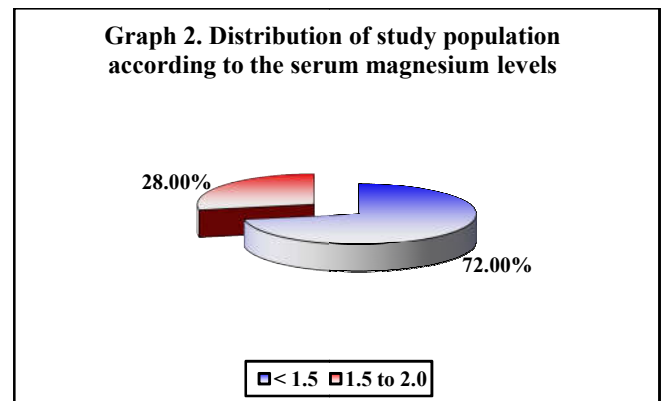


Table 2 Distribution of study population according to the serum magnesium levels

Serum magnesium (mg/dL)	Distribution (n=100)	
	Number	Percentage
< 1.5	72	72.00
1.5 to 2.0	28	28.00
Total	100	100.00



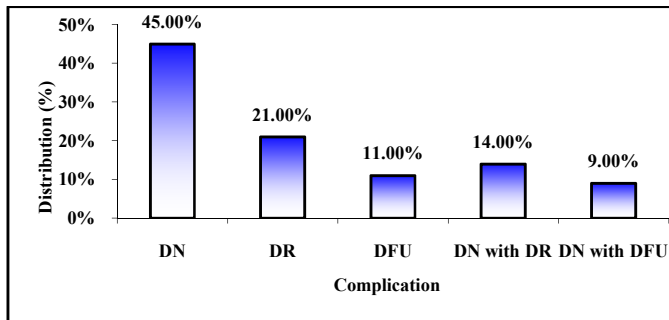
In this study the serum magnesium levels were low (< 1.5 mg/dL) in 72% of the diabetics. The mean serum magnesium levels were 1.32±0.27 mg/dL and median levels were 1.26 with range 0.8 to 2.0 mg/dL.

Table 3 Distribution of study population according to the complications

Complications	Distribution (n=100)	
	Number	Percentage
Diabetic Nephropathy (DN)	45	45.00
Diabetic retinopathy (DR)	21	21.00
Diabetic foot ulcer (DFU)	11	11.00
DN with DR	14	14.00
DN with DFU	9	9.00
Total	100	100.00

In the present study 45% of the patients had complications of diabetic nephropathy, diabetic retinopathy was noted in 21% of the patients and diabetic foot ulcer was present in 11% of the patient. However few patients presented with multiple complications that is 14% of the patients had diabetic nephropathy with diabetic retinopathy and 9% of the patients had diabetic nephropathy with diabetic foot ulcer. Overall, the complications of diabetic neuropathy were noted in 32%, diabetic retinopathy in 65% (PDR 3% and NPDR 32%) and diabetic foot ulcer in 20% of the patients.

Graph 3



DISCUSSION

Type 2 diabetes mellitus is one of the major global health challenges encountered in physicians practice in 21st century and associated with it are its complications subdivided into microvascular (retinopathy, neuropathy, nephropathy) and macrovascular complications [coronary artery disease (CAD), peripheral arterial disease (PAD), cerebrovascular disease].[10]Magnesium is the fourth most abundant cation in the human body and the second most abundant intracellular cation. Nevertheless, serum magnesium concentration though less sensitive, is a highly specific indicator of low magnesium status. The low serum magnesium levels in diabetics may contribute to the evolution of diabetic complications such as retinopathy, abnormal platelet function, cardiovascular disease and hypertension via reduction in the rate of inositol transport and subsequent intracellular depletion. Patients with severe diabetic retinopathy have lower magnesium levels which suggests that hypomagnesaemia may be a risk factor in development of diabetic retinopathy.[10] Hypomagnesaemia in patients with type 2 diabetes mellitus is frequently under-diagnosed and under-evaluated due to its usual asymptomatic presentation. Hence, this study was aimed to evaluate the serum magnesium levels in patients with type 2 DM and further to correlate with its complications.

In this study age ranged between range 35 to 80 years. The most common age group was 51 to 60 years comprised of 41% of the patients. The mean age was 55.26 ± 9.32 years and median age was 55 years suggesting involvement of middle age group. Apraci D. *et al.*[11] in their recent study reported mean age as 55.6 ± 10.4 years which was consistent with the present study.

In this study the serum magnesium levels ranged between 0.8 to 2.0 mg/dL. Majority of the diabetics (72%) had lower serum magnesium levels (< 1.5 mg/dL). The mean serum magnesium levels were 1.32 ± 0.27 mg/dL. These findings suggest that, hypomagnesemia is widely prevalent among diabetics and every second diabetic patient was diagnosed to have hypomagnesemia. Marked magnesium deficiency has been reported in the previous studies in patients with type-2 diabetes.[12-16] However, some workers have also reported normal levels.[17] According to CARDIA study [18] (Coronary Artery Risk Development in young Adults) there was an inverse relationship between Mg intake and the incidence of diabetic.

In the present study 45% of the patients had complications of diabetic nephropathy, diabetic retinopathy was noted in 21% of the patients and diabetic foot ulcer was present in 11% of the patient. However few patients presented with multiple complications that is 14% of the patients had diabetic

nephropathy with diabetic retinopathy and 9% of the patients had diabetic nephropathy with diabetic foot ulcer. Overall, complications of diabetic neuropathy were noted in 32%, diabetic retinopathy in 65% (PDR 3% and NPDR 32%) and diabetic foot ulcer in 20% of the patients. Some authors have suggested that reduced Mg level could have a role in the pathogenesis of complications of diabetes. Serum Mg depletion has been reported in diabetic patients who had advanced retinopathy and poor glycemic control.[11]

Association between serum magnesium levels and diabetic nephropathy

In this study a definite association between diabetic nephropathy and lower serum magnesium levels was noted as significantly higher number of patients with diabetic nephropathy had lower serum magnesium levels compared to those with normal serum magnesium levels (80.88% vs 19.12%; $p=0.004$). These findings were consistent with study by Sajjan NB *et al.*[19] from Karnataka who reported that serum levels of Magnesium showed statistically significant difference when compared in healthy subjects & Diabetic nephropathy. Recently, Dasgupta *et al.*[20] from Assam also reported that, both microalbuminuria and macroalbuminuria were found at a higher incidence in the hypomagnesemia group compared with the normal group. Corsonello *et al.*[21] demonstrated that diabetic patients with microalbuminuria or clinical proteinuria showed a significant decrease in serum ionized magnesium compared with normoalbuminuria.

One of the potential pathophysiological mechanisms linking serum magnesium to microalbuminuria is an amplification of insulin resistance. It is said that low serum magnesium plays an important role in the pathogenesis of insulin resistance.[22] Other hypothesis such as oxidative stress is becoming increasingly recognized as an important causative factor for microalbuminuria.[23]

Association between serum magnesium levels and diabetic retinopathy

In the present study significantly higher number of patients (94.29%) with diabetic retinopathy had lower serum magnesium levels compared to those who had normal serum magnesium levels (5.71%) ($p < 0.001$). There was a significant difference in prevalence of hypomagnesemia in diabetics with retinopathy. Recently, Dasgupta A., *et al.*[20] from Assam reported higher incidence of retinopathy in the hypomagnesemia group (64% vs 45.8%). The existence of a close relationship between impaired magnesium balance and retinopathy was established by Fujii *et al.*[24] who found a marked depletion in plasma and erythrocyte magnesium levels in diabetic patients with advanced retinopathy. Although the theory of depletion in the rate of inositol transport has been proposed by Grafton *et al.*[25] as a possible mechanism to explain the association between diabetic retinopathy and hypomagnesemia, the exact reason remains obscure.

Association between serum magnesium levels and diabetic foot ulcer

In this study 20 patients had diabetic foot ulcer. Majority of them that is 19 (95%) patients had lower serum magnesium levels while only 1 (5%) patient had normal serum magnesium levels. This difference was statistically significant ($p=0.010$) suggesting positive association between serum magnesium levels and diabetic foot ulcer. These findings were consistent

with a study by Keşkek SO *et al.* who detected a strong association between low magnesium levels and diabetic foot ulcers.[26]

Considering the pathophysiological mechanisms, it can be said that low serum magnesium concentration is a risk factor for developing type 2 DM, and that type 2 DM is one of the causes of hypomagnesaemia. Hypomagnesaemia can worsen the glycaemic control in DM, and both micro- and macrovascular complications of diabetes are strongly associated with hyperglycaemia and/or uncontrolled glycaemia.

CONCLUSIONS

In our case study, the relationship between the serum magnesium and complications of diabetes were found. 100 type 2 diabetes mellitus patients with complications like diabetic retinopathy, nephropathy, and foot ulcers were included in our study.

- Haematological & biochemical parameters like haemoglobin, fasting and post prandial blood sugar, HbA1c, urine microscopy, and serum creatinine were done.
- Diabetic retinopathy was found by Ophthalmoscopy,
- Almost equal numbers of patients were males (51%) and females (49%) with male to female ratio of 1.04:1.
- Most of the patients (41%) were aged between 51 to 60 years and the mean age was 55.26±9.32 years.
- The fasting blood sugar levels were > 110 mg/dL in majority (84%) of the diabetics and the mean fasting blood sugar levels were 198.17±99.35 mg/dL. Also majority of the patients (91%) had post prandial blood sugar levels were of >140 mg/dL and the mean post prandial blood sugar levels were 255.76±99.36 mg/dL and median levels. With regard to glycemic control, most of the diabetics (64%) had HbA1c levels of > 8.5 percent and the mean HbA1c levels were noted as 10.00±2.67 percent.
- The serum magnesium levels were low (<1.5 mg/dL) in 72% of the diabetics. The mean serum magnesium levels were 1.32±0.27 mg/dL.
- 45% of the patients had complications of diabetic nephropathy, 21% of the patients had diabetic retinopathy and diabetic foot ulcer was present in 11% of the patient.
- 80.88% patients with diabetic nephropathy had lower serum magnesium levels while 19.12% patients had normal serum magnesium levels. This difference was statistically significant (p=0.004).
- In patients with diabetic retinopathy, majority of the patients (94.29%) had lower serum magnesium levels and only 5.71% patients had normal serum magnesium levels. This difference was statistically significant (p< 0.001).
- Also majority of the patients (95%) with diabetic foot ulcer had lower serum magnesium levels and only 5% of the patients had normal serum magnesium levels. This difference was statistically significant (p=0.010).

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