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Serum magnesium in type 2 diabetic patients with microalbuminuria and overt proteinuria

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Abstract:
Introduction:*Magnesium is an essential mineral for the human body, principally because of its role in the regulation of cellular processes and its function as a cofactor in a wide range of metabolic reactions. Alterations in the distribution of magnesium within the body have been associated with several diseases, especially diabetes mellitus. Since hypomagnesemia has been reported to be directly related to the development of complications of type 2 diabetes mellitus, it is prudent to identify the condition and treat it, in an attempt to retard the progress of the complications of type 2 diabetes mellitus.*
Aim*: 1) Estimating serum magnesium levels in patients with type 2 diabetes mellitus.2) Comparing mean magnesium levels in type 2 diabetic patients with normoalbuminuria, microalbuminuria and overt proteinuria*.
Methods: *A total of 60 previously diagnosed type 2 diabetes mellitus patients admitted in M S Ramaiah Hospital during the period September 2012 to September 2014 formed the study population considering the inclusion and exclusion criteria. The study population was grouped in the following groups – Normoalbuminuria, microalbuminuria and overt proteinuria based on 24 hour urine albumin excretion.*
Results:*The mean magnesium level in the study population (n=60) was 1.85±0.34 mg/dl. The mean magnesium levels in the over proteinuria group (n=20) was found to be lower (1.57±0.17 mg/dl) compared to the microalbuminuria group (n=20) (1.90±0.21 mg/dl) and more so in the normoalbuminuria group (n=20) (2.10±0.37 mg/dl). The correlation was statistically significant (P<0.001).*
Conclusion: *In this study, it was observed that microalbuminuria, overt proteinuria along with poor glycemic control are associated with lower levels of serum magnesium. This association was also observed with increasing severity of diabetic retinopathy. Since hypomagnesemia has been linked to worsening of complications of diabetes mellitus, efforts to minimize hypomagnesemia in the management of type 2 diabetes are warranted. Identifying and treating hypomagnesemia can potentially delay end stage renal disease in diabetic nephropathy.*
Key words:*Type 2 Diabetes Mellitus, microalbuminuria, proteinuria, diabetic nephropathy, glycosylated hemoglobin, magnesium.*

I. Introduction

Diabetes mellitus (DM) refers to a group of common metabolic disorders that share the phenotype of hyperglycemia. Several distinct types of DM are caused by a complex interaction of genetics and environmental factors. Depending on 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 that impose a tremendous burden on the individual with diabetes and on the health care system.[1]

Type 2 diabetes mellitus is on track to become one of the major global public health challenges of the 21st century.[2] Diabetes is fast gaining the status of a potential epidemic in India, with more than 62 million diabetic individuals currently diagnosed with the disease[3] and it is predicted that by 2030 diabetes mellitus may afflict up to 79.4 million individuals in India.[4]

Magnesium (Mg), is one of the most abundant intracellular ions with an essential role in fundamental biological reactions, whose deficiency provokes biochemical and symptomatic alterations in the human organism.[5] The concentrations of magnesium in serum of healthy people are remarkably constant, whereas 25-39% of diabetics have low concentrations of serum magnesium.[6] Hypomagnesemia has been related as a cause of insulin resistance, also being a consequence of hyperglycemia, and when it is chronic leads to macrovascular and micro-vascular complications of diabetes, worsening the deficiency of magnesium.[7] The association of hypomagnesemia with Diabetes Mellitus works the other way as well, hypomagnesemia independently predicts the progression to End stage renal disease in patients with advanced type 2 diabetic nephropathy.[8]

The present study was undertaken with the objective to estimate the serum magnesium concentrations in type 2 diabetic patients and how the levels correlated with diabetic nephropathy.

Aims and objectives

1. Estimating serum magnesium levels in patients with type 2 diabetes mellitus.

2. Comparing mean magnesium levels in type 2 diabetic patients with normoalbuminuria, microalbuminuria and overt proteinuria

II. Materials and Methods

A total of 60 randomly selected patients of type 2 diabetes mellitus admitted in M S Ramaiah Hospital during the period September 2012 to September 2014 were taken considering the inclusion and exclusion criteria.

Methods of collecting data

- Structured preformat
- Detailed history with duration of disease, treatment & co-morbidities
- Detailed general and systemic examination
- Height, weight, waist circumference and hip circumference measurements
- Fundus examination
- 24 hour urine albumin
- Urine routine
- Blood samples for magnesium, FBS, PPBS, HbA_1C, serum creatinine, serum albumin, lipid profile

Inclusion criteria: Type 2 Diabetes mellitus patients aged >18 years.

Exclusion criteria:

1. Type 1 Diabetes Mellitus
2. Alcohol abuse
3. UTI/Pyelonephritis
4. Patients on magnesium based antacid medication
5. Patients on long term diuretics
6. Patients with Malabsorption or chronic diarrhea
7. Bed ridden patients
8. Patients on dialysis

Statistical methods

Descriptive and inferential statistical analysis was been carried out in the present study. Results on continuous measurements were presented on Mean ± SD (Min-Max) and results on categorical measurements were presented in number (%). Significance was assessed at 5 % level of significance. Analysis of variance (ANOVA) has been used to find the significance of study parameters between three or more groups of patients. Student-t test (two tailed, independent) was been used to find the significance of study parameters on continuous scale between two groups (Inter group analysis) on metric parameters. Chi-square/ Fisher Exact test were used to find the significance of study parameters on categorical scale between two or more groups.

III. Results

The mean age of the study population was 57.15±10.17(Table 1) with 63.8% being men.The mean serum magnesium in the Normoalbuminuria group was 2.10±0.37 mg/dl, in the microalbuminuria group it was significantly lower (1.90±0.21 mg/dl) and value was the lowest in the overt proteinuria group (1.57±0.17 mg/dl) (Fig. 1). 95% of patients with overt proteinuria had serum magnesium levels <1.80 mg/dl (Fig. 2). It was observed in the study population that the mean GFR was lower as the severity of nephropathy increased (Fig. 3).The mean duration of diabetes was significantly higher in the overt proteinuria group compared to the microalbuminuria and normoalbuminuria group (Table 2), similarly the glycemic control too was poorer in patients with established nephropathy compared to the normoalbuminuria group. HbA1c was highest among patients with overt proteinuria and lowest among patients with normoalbuminuria (Table 3).

Table 1: Age distribution of patients

Age in years	Normoalbuminuria (n=20)	Microalbuminuria (n=20)	Overt proteinuria (n=20)	Total (n=60)
38-40	2	0	0	2
41-50	9	6	2	17
51-60	8	5	7	20
61-70	1	4	7	12
71-80	0	5	4	9
Mean ± SD	49.50±6.68 years	59.75±10.87 years	62.20±7.92 years	57.15±10.17 years

Table 2: Duration of Diabetes Mellitus of patients studied

Duration of DM	Normoalbuminuria (n=20)	Microalbuminuria (n=20)	Overt proteinuria (n=20)	Total (n=60)
≤5	13	6	2	21
5-10	5	5	8	18
11-20	2	8	7	17
21-40	0	1	3	4
Mean ± SD	5.10±3.11 years	10.10±6.47 years	12.35±7.29 years	9.18±6.56 years

Table3 – Glycemic control in the 3 groups studied and correlation with serum magnesium level

Glycemic control	Normoalbuminuria (n=20)	Microalbuminuria (n=20)	Overt proteinuria (n=20)	Total (n=60)
HbA1c	8.09±1.27	9.22±1.56	10.19±1.35	9.16±1.62
Serum Magnesium (mg/dl)	2.10±0.37	1.90±0.21	1.57±0.17	1.85±0.34

Figure 1: Comparison of Serum Magnesium in three groups studied

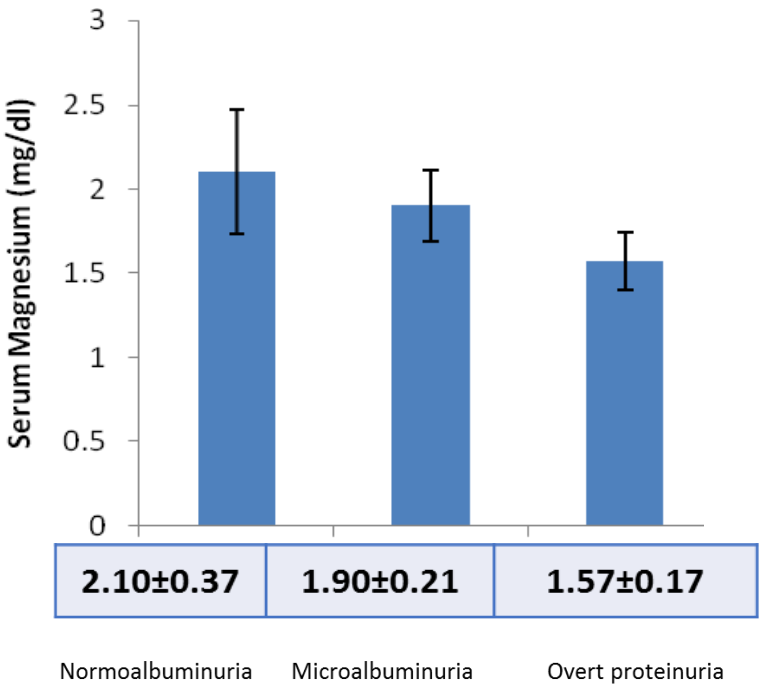


Figure 2: Comparison of low magnesium with high magnesium in the 3 groups studied

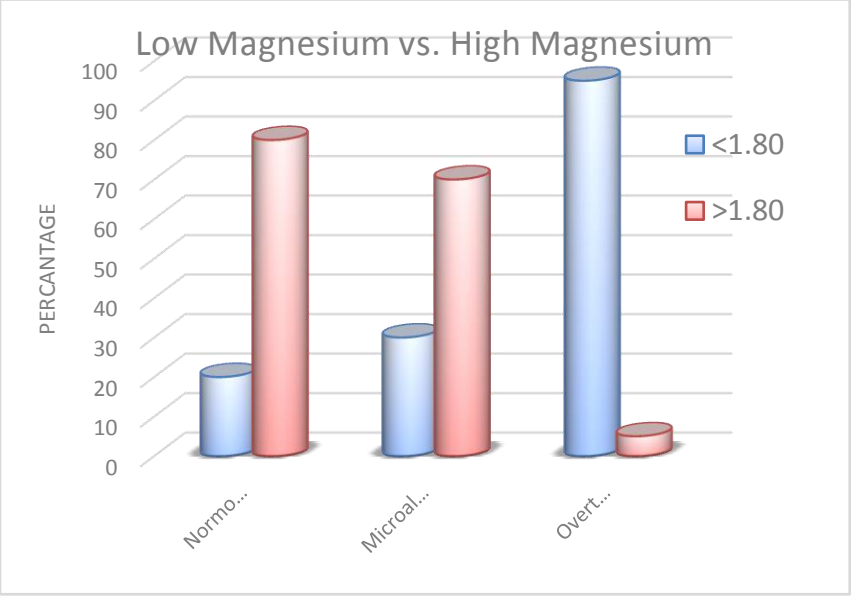
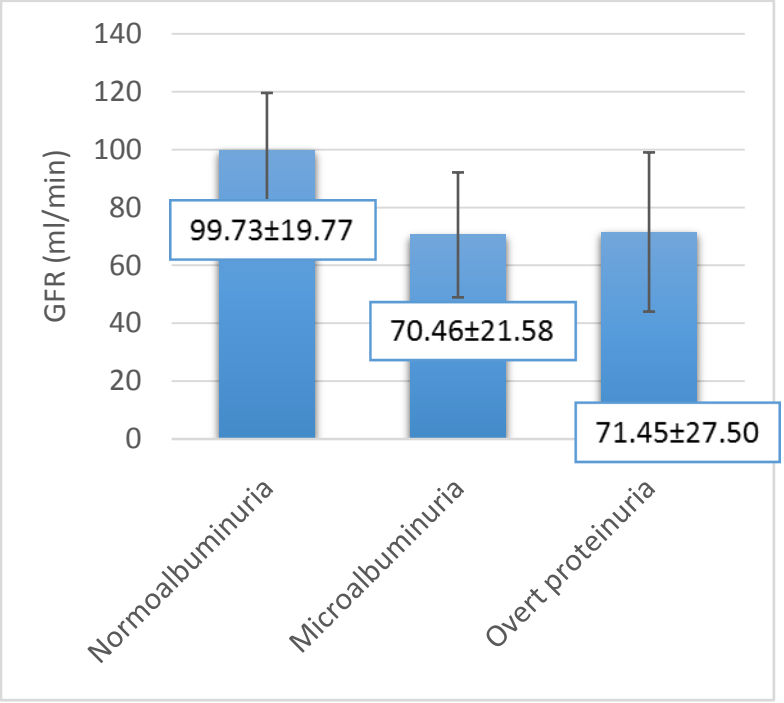


Figure 3: Comparison of GFR in three groups studied



IV. Discussion

Type 2 diabetes accounts for approximately 90 to 95% of all diagnosed cases of diabetes.In addition to hyperosmolar coma and ketoacidosis, patients with type 2 diabetes may have cardiovascular disease, nephropathy, retinopathy, and neuropathy. The treatment of the patients with diabetes requires a multidisciplinary approach whereby every potential complicating factor must be monitored closely and treated.

Hypomagnesemia has been reported to occur with increased frequency among patients with type 2 diabetes as compared with their counterparts without diabetes. Despite numerous reports linking hypomagnesemia to chronic diabetic complications, attention to this issue is lacking among clinicians. This study was aimed at determining the serum magnesium concentration in diabetic population and correlating it with various stages of diabetic nephropathy.

Hypomagnesemia, has been reported to occur in 13.5 – 47.7% of non-hospitalized patients with type 2 diabetes compared with 2.5 – 15% among their counterparts without diabetes.[9]

However, the evidence towards magnesium deficiency in diabetic patients has been well established. A large number of studies have been done over the last 50 years estimating serum magnesium in diabetic patients in comparison to healthy individuals. Most of those studies show a decreased serum magnesium concentration in the diabetic group compared to the control group, and in most cases the difference is significant.In some of the studies, although mean serum magnesium concentration was decreased in diabetic patients, they were still within the reference range. In our study, the normal range of serum magnesium was 1.7 – 2.5 mg/dl and the mean serum magnesium was 1.85±0.34 mg/dl, similar to those studies.[10]

Hypomagnesemia has been related as a cause of insulin resistance worsening the glycemic status of the patient. This relation also works the other way as hypomagnesemia is also a consequence of hyperglycemia. When hypomagnesemia is chronic, it leads to macro-vascular and micro-vascular complications of diabetes, in turn worsening the magnesium deficiency.[11]

According to a study conducted by Yusuke Sakaguchi et al in 2012, hypomagnesemia independently predicts the progression to End stage renal disease in patients with advanced type 2 diabetic nephropathy.[8]

Corsonello et al. in 2000 observed that the mean serum ionized magnesium levels were significantly reduced in diabetic patients with microalbuminuria or clinical proteinuria compared to the normoalbuminuria group.[12]

In our study the mean serum magnesium level in the normoalbuminuria group was 2.10±0.37 mg/dl, mean serum magnesium level in the microalbuminuria group was 1.90±0.21 mg/dl and only 1.57±0.17 mg/dl in the overt proteinuria group. These results were statistically significant and were similar to the aforementioned study, [12] although in our study total serum magnesium was measured rather than ionized serum magnesium.

A recent retrospective study[13]conducted by Pham PC et al in 2005 reported an association between low serum magnesium levels and a significantly faster rate of renal function deterioration in patients with type 2 diabetes.

Consequently, in the study[8]conducted by Yusuke Sakaguchi et al. in 2012, participants categorized into Low-magnesium (serum Mg <1.8 mg/dl) and High-Magnesium (serum Mg >1.8 mg/dl) groups showed that the Low-Magnesium group had a 2.12-fold higher risk of End stage renal disease than the High-Magnesium group (P = 0.004).In our study, it was observed that 80% of the patients in the normoalbuminuria group had a serum magnesium level of >1.80 mg/dl and 95% of the patients in the overt proteinuria group had a serum magnesium level of <1.80 mg/dl, indicating that a significant proportion of patients with low serum magnesium levels had overt proteinuria.

The mean duration of diabetes in our study was 9.18±6.56 years in the study population. The duration of diabetes was 5.10±3.11 years in the normoalbuminuria group, 10.10±6.47 years in the microalbuminuria group and 12.35±7.29 years in the overt proteinuria group. This finding was similar to a study[12] conducted by Corsonello et al. in 2000.

The mean BMI of the patients in our study was 26.46±3.35. In the normoalbuminuria group, the mean BMI was 25.49±3.31, 26.71±3.22 in the microalbuminuria group and 27.19±3.47 in the overt proteinuria group. These findings were also conformant to the study[12] done by Corsonello et al. in 2000.

It was also observed that the mean waist-hip ratios of the patients with established diabetic nephropathy (microalbuminuria and overt proteinuria groups) were higher compared to those without nephropathy. Similar findings were observed in a study[14] done by M Reid et al.

Numerous studies have reported an inverse relationship between glycemic control and serum magnesium levels.[15, 16]

Clinical studies evaluating the effect of supplemental magnesium on glycemic control are mixed, with some studies reporting improvements [17, 18]& others showing no improvement[19, 20]. Some of the inconsistencies among these studies can be explained by differences in treatment periods, doses of magnesium and parameters used to evaluate the effect.

Magnesium depletion has a negative impact on glucose homeostasis and insulin sensitivity in diabetic patients[21]as well as on the evolution of complications such as nephropathy, retinopathy, thrombosis and hypertension[22-24]. Preventing low magnesium status in diabetics may therefore be beneficial in the management of the disease.

In our study, the mean HbA1c in the normoalbuminuria group was lowest at 8.09±1.27%. In the microalbuminuria group it was 9.22±1.56% and in the overt proteinuria group it was 10.19±1.35%. There was a statistically significant negative correlation between serum magnesium and HbA1c.

In the present study, magnesium supplementation and its effects towards magnesium levels or metabolic control was not done. Hence the change in the magnesium status with respect to improvement or worsening of diabetic state in the long run needs to be studied.

V. Conclusion

The aims of this comparative three groups controlled study were to estimate serum magnesium levels in 60 patients with type 2 diabetes mellitus and comparing mean magnesium levels in these patients with normoalbuminuria, microalbuminuria and overt proteinuria.

In this study, it was observed that microalbuminuria, overt proteinuria along with poor glycemic control are associated with lower levels of serum magnesium. Since hypomagnesemia has been linked to worsening of microvascular and macro-vascular complications of diabetes mellitus, efforts to minimize hypomagnesemia in the management of type 2 diabetes are warranted.

Magnesium measurement may represent a sensitive indicator of the magnesium homeostasis disturbances in type 2 diabetic patients with different grades of diabetic nephropathy.Considering the results of this study as well as those done earlier, identifying and treating hypomagnesemia can potentially delay end stage renal disease in diabetic nephropathy.

The potential benefits of supplementing magnesium in type 2 diabetic patients with hypomagnesemia needs to be evaluated further.

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