

## Original Research Article

# Serum magnesium levels in newly diagnosed type 2 diabetes mellitus and its relation with microvascular complications of diabetes

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### ABSTRACT

**Background:** Prevalence of hypomagnesaemia is significantly higher in diabetic patients with microvascular complications compared to diabetics with no microvascular complications. The aim of this study is to measure levels of serum magnesium in patients with newly diagnosed type 2 diabetes mellitus and study its association with the presenting microvascular complications.

**Methods:** This was hospital based, one year cross-sectional study carried out in Department of Medicine, IGMC Shimla in patients with newly diagnosed type 2 diabetes mellitus. Total 53 patients were enrolled in this study who presented in medicine OPD or admitted in medicine ward.

**Results:** Serum Magnesium value of the patients ranged from 1.20-3.0 mg/dl with mean value of  $1.9 \pm 0.3$  mg/dl. Fourteen patients (26.4%) had hypomagnesaemia. A total of 34 (64.2%) patients presented with complications of diabetes in which proteinuria was present in 34 (64.2%), retinopathy in 4 (7.5%) and neuropathy in 1 (1.9%). Fourteen (41.2%) patients with hypomagnesaemia presented with complications of diabetes ( $p$  value=0.003). 34 (64.2%) patients presented with proteinuria out of which 14 (41.2%) patients had hypomagnesaemia while 20 (58.8%) had normomagnesaemia ( $p=0.03$ ). One (1.9%) patient had neuropathy and hypomagnesaemia was also present in this patient ( $p=0.6$ ). Four patients (7.5%) presented with retinopathy out of which 3 (5.7%) had hypomagnesaemia while 1 (1.9%) had normomagnesaemia.

**Conclusions:** Hypomagnesaemia is associated with microvascular complications of diabetes. Also there is statistically significant relationship between proteinuria and hypomagnesaemia in patients with newly diagnosed type 2 diabetes mellitus.

**Keywords:** Hypomagnesaemia, Microvascular complications, Proteinuria, Type 2 diabetes mellitus

### INTRODUCTION

Diabetes mellitus refers to a group of common metabolic disorders that share the common phenotype of hyperglycemia. Depending on etiology of the diabetes mellitus factors contributing to hyperglycaemia include reduced insulin secretion, decreased glucose utilization, and increased glucose production. Diabetes mellitus is one of the most common metabolic disorders and leading cause of death and disability in the world. The worldwide prevalence of diabetes mellitus has risen dramatically

over the past two decades, from an estimated 30 million cases in 1985 to 382 million in 2013.<sup>1</sup>

Magnesium is an electrolyte of chief physiological importance in the body, being the most abundant divalent intracellular cation in the cells, the second most abundant cellular ion next to potassium and the fourth cation in general in the human body. The kidneys help to maintain the normal plasma levels of magnesium between 1.7 and 2.4 mg/dl. Approximately 50% of body magnesium is in bones and is not readily available as a dynamic reservoir

for use in other body tissues. A small part of magnesium is in the extracellular fluid compartment.

Diabetes has shown to be associated with abnormalities in the metabolism of zinc, chromium, copper, magnesium and manganese.<sup>2</sup>

Magnesium deficiency is found to be commonly associated with endocrine and metabolic disorders, especially with diabetes mellitus. Na/K-ATPase is involved in the maintenance of gradients of Na<sup>+</sup> and K<sup>+</sup> and glucose transport. Na/K-ATPase plays an important role in the development of diabetic nephropathy. Magnesium deficiency affects the activity of Na/K-ATPase. Magnesium deficiency augments intracellular inositol depletion, which results in reduced activity of regulatory proteins and leads to diabetic nephropathy.<sup>3</sup>

Prevalence of hypomagnesaemia is significantly higher in diabetic patients with microvascular complications compared to diabetics with no microvascular complications. Prevalence of hypomagnesaemia is significantly higher in patients with diabetic retinopathy.<sup>4</sup>

Studies have shown that low serum magnesium was associated with diabetic retinopathy. Studies have also shown that there is a strong association between low serum magnesium level and development of foot ulcers in diabetes.<sup>5</sup>

Arundhati Dasgupta et al, conducted a cross sectional study in 150 patients and found that hypomagnesaemia was found to be associated with poor glycemic control and increased incidence of retinopathy, nephropathy and foot ulcers.<sup>6</sup>

Dipankar Kundu et al, conducted a study in which they concluded that hypomagnesaemia and albuminuria individually or in conjunction serve as indicators for dysglycemia and they could be used as marker for the risk of development of diabetic retinopathy.<sup>7</sup>

Dr Sarah S Premraj et al, studied the level of serum magnesium in type 2 diabetic patients and correlated serum magnesium concentration with microvascular complications in these patients. They concluded that hypomagnesaemia was associated with microvascular complications in patients with type 2 diabetes mellitus.<sup>8</sup>

Saprou N et al, studied serum magnesium levels in patients with type 2 diabetes mellitus and correlated it with complications of type 2 diabetes mellitus. They found that the prevalence of hypomagnesaemia in type 2 diabetes was 30%. This study also showed that as the magnesium level decreases in type 2 diabetic patients, prevalence of retinopathy increases.<sup>9</sup>

The aim of this study is to measure levels of serum magnesium in patients with newly diagnosed type 2

diabetes mellitus and study its association with the presenting microvascular complications.

## METHODS

This was hospital based, one year cross-sectional study carried out in Department of Medicine, IGMC, Shimla, Himachal Pradesh (a tertiary care hospital) in patients with newly diagnosed type 2 diabetes mellitus. During 1<sup>st</sup> October 2017 to 30<sup>th</sup> September 2018.

Detailed history, clinical examination and biochemical investigations including patient's age, sex, details regarding presenting complaints, past history of any other diseases, history of co-morbid diseases like hypertension, ischemic heart disease were taken.

Pulse rate, blood pressure, respiratory rate, temperature, height, weight, BMI and detailed systemic examination was carried out in all patients and proforma of each patient was filled.

Diagnosis of diabetic neuropathy was made by a detailed medical history and neurological examination by testing for pinprick sensation test, perception with monofilaments, vibration and position sense and deep tendon reflexes. Diabetic retinopathy was diagnosed with fundus examination, performed by an ophthalmologist. Proteinuria was diagnosed by measuring 24 hour urinary proteins.

Fasting serum magnesium was done in SRL lab at IGMC Shimla by spectrophotometric method. The reference value of serum Mg<sup>2+</sup> was between 1.9-2.5 mg/dl. Other relevant investigations were also done in all patients in SRL lab at IGMC Shimla.

### Inclusion Criteria

- All newly diagnosed patients of type 2 diabetes mellitus presented in medicine OPD or admitted in medicine ward.

### Exclusion Criteria

- Patients on drugs that affect magnesium levels (diuretics, aminoglycosides, amphotericin B, etc)
- Malabsorption or diarrhea
- Alcohol consumption
- Vitamin or mineral supplements in recent past
- Pregnancy
- Lactation
- Sepsis.

Patients were divided in two groups

- Type 2 diabetics without hypomagnesaemia.
- Type 2 diabetics with hypomagnesaemia.

Each group was further subdivided into

- Patients not having microvascular complications.
- Patients having neuropathy.
- Patients having nephropathy in the form of albuminuria or proteinuria.
- Patients having retinopathy.

**RESULTS**

Patients were divided into different age groups. Most of the patients belongs to the age group of 41-50 years, constituting around 35.8% of total 53 patients. As per the sex distribution of the patients in this study, male and female patients were almost equal. Female were 27 and male 26 in number.

After physical examination of the patients, mean pulse rate of the patients was 86 bpm. Mean SBP of the patients was 126 mmHg and mean DBP was 80 mmHg. The mean weight of the patients was 65.4 Kg, mean height was 162.3 cm and mean BMI was 24.9 Kg/cm<sup>2</sup>.

Hemoglobin of the patients ranged between 10.4-19.0 gm/dl with the mean being 14.5±1.9. FBS of the patients ranged between 124-497 mg/dl with the mean of 218.9±84.3. PPBS ranged between 203-518 mg/dl with the mean of 313.3±85.4. HbA<sub>1c</sub> of the patients ranged between 6.6-17.5% with the mean of 10.0±2.7. Blood urea nitrogen value of the patients ranged between 8-28 mg/dl with the mean of 14.1±4.4. Serum creatinine value of the patients ranged between 0.24-1.30 mg/dl with the mean being 0.8±0.2.

Serum magnesium value of the patients ranged from 1.2-3.0 mg/dl with the mean value of 1.9±0.3 mg/dl.

Serum cholesterol value of the patients ranged between 122-296 mg/dl with the mean value of 180.2±50.8. Triglyceride value of the patients ranged between 136-542 mg/dl with mean being 167.8±80.6. HDL value of the patients ranged between 23-70 mg/dl with the mean of 41.7±9.5. LDL value of patients ranged between 42-262 mg/dl with the mean being 117.3±43.2.

Among 24 hour urine proteins value of patients ranged between 15-1580 mg/day with the mean being 223.7±345.8.

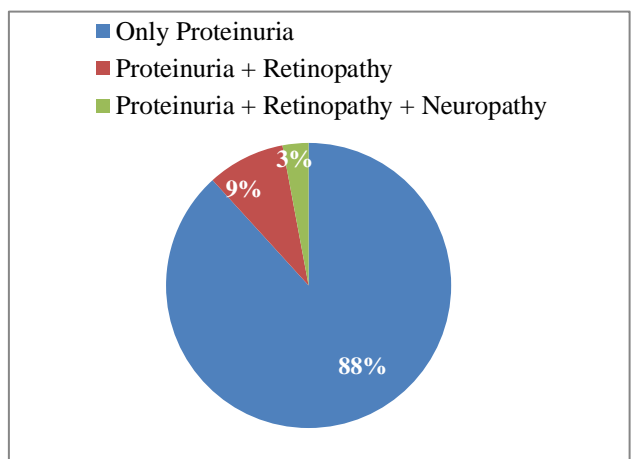
Out of 53 patients, 34 (64.2%) patients presented with microvascular complications of diabetes mellitus. Out of these 34 patients, 30 (88.3%) had only proteinuria, 3 (8.8%) had both proteinuria and retinopathy and 1 (2.9%) had proteinuria, retinopathy and neuropathy. (Table 1 and Figure 1).

Correlation of serum magnesium levels with presenting microvascular complications of diabetes was studied. (Table 2). Out of 53 patients, 39 (73.6%) patients had

normomagnesaemia while 14 (26.4%) patients presented with hypomagnesaemia. A total of 34 (64.2%) patients presented with microvascular complications of diabetes. Among them 20 (37.8%) patients had normomagnesaemia while 14 (26.4%) patients had hypomagnesaemia. Thus 14 (26.4%) patients with hypomagnesaemia presented with microvascular complications of diabetes (p value=0.003).

**Table 1: Distribution of different presenting complications of diabetes mellitus in patients.**

Complications	Frequency	Percentage
Only Proteinuria	30	88.3
Proteinuria + Retinopathy	3	8.8
Proteinuria + Retinopathy + Neuropathy	1	2.9



**Figure 1: Distribution of different microvascular complications of diabetes mellitus in patients.**

**Table 2: Correlation of serum magnesium levels with presenting microvascular complications of diabetes.**

S. Magnesium	Microvascular complications (n=53)		P value
	Absent(%)	Present(%)	
Normal	19 (35.8)	20 (37.8)	0.003
Hypomagnesaemia	0 (0.0)	14 (26.4)	

Correlation of serum magnesium levels with proteinuria was studied (Table 3). Out of 53 patients, 34 (64.2%) patients presented with proteinuria. 14 (26.4%) patients with proteinuria had hypomagnesaemia while 20 (37.7%) had normomagnesaemia (p=0.03). In hypomagnesaemia group, 9 (64.3%) patients had microalbuminuria while 5 (35.7%) had macroalbuminuria.

Correlation of serum magnesium levels with neuropathy was studied (Table 4). Out of 53 patients, only 1 (1.9%) patient had neuropathy and hypomagnesaemia was also present in this patient (p=0.6).

Correlation of serum magnesium levels with retinopathy was studied. Out of 53 patients, 4 patients (7.5%) presented with retinopathy. 3 (5.7%) patients with retinopathy had hypomagnesaemia while 1(1.9%) patient had normal magnesium levels ( $p=0.09$ ) (Table 5).

**Table 3: Correlation of serum magnesium levels with proteinuria.**

S. Magnesium	Proteinuria (N=53)		p value
	Absent(%)	Present(%)	
Normal	19 (35.8)	20 (37.7)	0.03
Hypomagnesaemia	0 (0.0)	14 (26.4)	

**Table 4: Correlation of serum magnesium levels with neuropathy.**

S. Magnesium	Neuropathy (N=53)		p value
	Absent(%)	Present(%)	
Normal	39 (73.6)	0 (0.0)	0.6
Hypomagnesaemia	13 (24.4)	1 (1.9)	

**Table 5: Correlation of serum magnesium levels with retinopathy.**

S. Magnesium	Retinopathy(N=53)		p value
	Absent(%)	Present(%)	
Normal	38 (71.7)	1 (1.9)	0.09
Hypomagnesaemia	11 (20.7)	3 (5.7)	

## DISCUSSION

This study enrolled a total of 53 patients of newly diagnosed type 2 diabetes mellitus. Out of 53 patients, 34 (64.2%) patients presented with microvascular complications of diabetes mellitus. Out of these 34 patients, 30 (88.3%) had only proteinuria, 3 (8.8%) had both proteinuria and retinopathy and 1 (2.9%) had proteinuria, retinopathy and neuropathy. In this study, 34 (64.2%) had nephropathy in the form of proteinuria. 21 (61.8%) were female while 13 (38.2%) were male.

Serum magnesium value of the patients ranged from 1.20-3.0 mg/dl with mean value of  $1.9\pm 0.3$ . In a study conducted by Arpaci D et al, the mean magnesium level was  $1.97\pm 0.25$  (1.13-3.0) mg/dl which was almost similar to this study.<sup>10</sup> In another study conducted by Dr Sarah S Premraj et al, the mean serum magnesium level was  $1.96\pm 0.18$  mg/dl which is also comparable to this study.<sup>8</sup>

In this study, 39 (73.6%) patients had normal magnesium level while 14 (26.4%) patients presented with hypomagnesaemia. In a study conducted by Saproo N et al, 30 (30%) patients had hypomagnesaemia which is almost comparable to this study.<sup>9</sup>

A total of 34 (64.2%) patients presented with complications of diabetes. Out of these 34, 20 (58.8%) patients had normal magnesium level while 14 (41.2%)

patients had hypomagnesaemia. Thus 14 patients with hypomagnesaemia presented with complications of diabetes ( $p$  value=0.003) which is statistically significant. Dr Sarah S Premraj et al, also found a statistically significant correlation between hypomagnesaemia and microvascular complications of diabetes.<sup>8</sup>

The association between proteinuria and depletion of magnesium is controversial. In this study, out of 53 patients, 34 (64.2%) patients presented with proteinuria. Out of these, Fourteen (41.2%) patients had hypomagnesaemia while 20 (58.8%) patients had normomagnesaemia ( $p=0.03$ ). In hypomagnesaemia group, 9 (64.3%) patients had microalbuminuria while 5 (35.7%) had macroalbuminuria. Thus all the patients who presented with hypomagnesaemia had proteinuria which is statistically significant. Arpaci D et al, concluded in their study that 26 (3.8%) of the patients with hypomagnesaemia had proteinuria.<sup>10</sup> They found that serum magnesium was inversely associated with the prevalence of proteinuria. Dr Sarah S Premraj et al, also observed significant inverse relationship between serum magnesium level and proteinuria.<sup>8</sup> However, Zargar et al, found that there was no relationship between glycemic control and microalbuminuria with serum magnesium level.<sup>11</sup> Other studies also have not found any association between serum magnesium and proteinuria in Type 1 and Type 2 diabetes.<sup>11,12</sup>

Out of 53 patients, only 1 (1.9%) patient had neuropathy and hypomagnesaemia was also present in that patient ( $p=0.6$ ). However, in the study conducted by Saproo N et al, they observed neuropathy in 11 (22.9%) of patients. This could be due to the reason that the study conducted by Saproo N et al, was not done in newly diagnosed type 2 diabetes mellitus and the incidence of neuropathy increases with duration of diabetes.<sup>9</sup> Out of 53 patients, 4 patients (7.5%) presented with retinopathy. Out of these 4 patients, 3 (5.7%) patients had hypomagnesaemia while 1 (1.9%) patient had normal magnesium levels ( $p=0.09$ ). However, in a study conducted by Saproo N et al, they observed retinopathy in 29 (60.4%) patients and there was inverse relationship between serum magnesium level and retinopathy.<sup>9</sup> Arpaci D et al, found that there was no relation between magnesium level and retinopathy. Thus the relationship of hypomagnesaemia with diabetic retinopathy is controversial.<sup>1</sup>

The limitation of our study is that it is a single-centre study with a relatively limited number of patients constituting a sample. As in order to ensure the homogenous sample and to eliminate the possible external confounding factors we need to have an optimum sample size.

## CONCLUSION

The study results suggest that all those patients who had hypomagnesaemia in newly diagnosed type 2 diabetes mellitus were having microvascular complications and



there is statistically significant correlation between hypomagnesaemia and microvascular complications of diabetes. Also all the patients who presented with hypomagnesaemia had proteinuria and there is statistically significant relationship between proteinuria and hypomagnesaemia in patients with newly diagnosed type 2 diabetes mellitus. There is also association of hypomagnesaemia with neuropathy and retinopathy in newly diagnosed type 2 diabetes mellitus but this relationship was not statistically significant in this study. So in this study, hypomagnesaemia was strongly associated with microvascular complications of type 2 diabetes mellitus. Further large scale studies are needed in order to determine whether the correction of magnesium deficiency could be effective in the prevention of diabetes mellitus, and to reduce the incidence of microvascular complications and to further elucidate the association between serum magnesium and microvascular complications.

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