



RESEARCH ARTICLE

STUDY OF SERUM MAGNESIUM IN TYPE 2 DIABETES MELLITUS

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ABSTRACT

Background: Diabetes Mellitus is one of the most common metabolic disorder and leading cause of death & disability in the world. It is due to absolute or relative insulin deficiency which leads to increased blood glucose level. Magnesium is a crucial co-factor for many enzymatic reactions involved in metabolic process. So Mg depletion has negative impact on glucose homeostasis and insulin sensitivity. Magnesium deficiency also results in failure to inhibit entry of calcium into myocardial cells, failure to extrude Ca from the cells and failure of sarcoplasmic reticulum to sequester excess Ca. Mg deficiency is typical in chronic, stable mild type 2 DM and may be a strong predisposing factor for development of complications such as retinopathy, thrombosis and hypertension and also for the development of excess cardiovascular morbidity associated with diabetes.

Objectives: Aim of this study was to compare the serum Magnesium concentration in patients with type 2 Diabetes Mellitus and non-diabetes controls to assess its impact on complications.

Primary objective: To estimate the diabetic profiles - FBS, PPBS and HbA_{1c} along with Magnesium and Calcium profiles in diabetes cases and non-diabetes controls.

Method: The current study population included age matched 115 patients i.e., 75 cases who attended the Diabetic clinic and 40 controls who attended the out-patient wing of General Medicine during the study period. After getting written consent, blood samples for estimation of different parameters were collected. Serum samples were used to estimate urea, creatinine, plasma concentration of glucose (both fasting as well as postprandial), serum Magnesium, serum calcium & concentration of HbA_{1c} in EDTA blood samples were also estimated.

Result: The mean serum Mg levels were lower in diabetic patients (1.59±0.242 mg/dL). The age group 61-70 reported higher the number of low Mg levels. Diabetic females showed low levels of Mg than in diabetic males. According to duration of diabetes majority of low Mg levels were seen in patients who had diabetes for >7 years. The correlative studies of magnesium with age and duration of diabetes both showed a suggestive negative correlation with $r = -0.240$, $p = 0.001$ and $r = -0.409$, $p = 0.001$ respectively and a moderate negative significant correlation with r values -0.733 , -0.706 and -0.780 respectively were obtained between serum Mg with FBS, PPBS and HbA_{1c}. A moderate positive significant correlation with $r = +0.647$ and $p = 0.001$ was obtained between serum Mg with serum Ca.

Conclusion: Low Mg in the diabetic patient were correlated with hypertension with predominant associated complications such as Diabetic Retinopathy, Diabetic Neuropathy and Cellulitis. In hypomagnesaemia diabetic patients higher levels of HbA_{1c} indicate the risk of development of diabetic complications. Preventing hypomagnesaemia in Diabetes Mellitus by supplementing Mg is helpful in increasing insulin sensitivity and delaying the development of diabetic complications.

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INTRODUCTION

Diabetes mellitus is the most common metabolic disorder. Around 415 million across the world are living with diabetes, out of which over 69 million are Indians (International Diabetes Federation, 2015). Insulin resistance is the hallmark in development of type 2 diabetes mellitus especially in India. Magnesium being the crucial co-factor for various enzymatic

reactions involved in metabolic reaction, its depletion has reported to have increased peripheral insulin resistance (Barbagallo *et al.*, 2007). Further, the decrease in magnesium level can lead to diabetes complications such as retinopathy, thrombosis and hypertension (Kulkarni *et al.*, 2014). The deficiency of Mg can also result in failure to inhibit calcium entry into myocardial cells, failure to extrude Ca from the cells and failure of sarcoplasmic reticulum to sequester excess Ca (Barbagallo *et al.*, 2007). Preventing hypomagnesaemia in diabetes mellitus by supplementing Mg may be helpful in increasing insulin sensitivity and delaying the development of diabetic complications.

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Hence we have designed a study to compare the serum Mg concentration in patients with type 2 diabetes mellitus (T2DM) and non-diabetes controls, and to assess the impact of Mg concentration on diabetes complications.

MATERIALS AND METHODS

A single-centric, hospital based, cross-sectional study was conducted for 6 months in Diabetic Clinic, Medical College Hospital, Government Medical College, Trivandrum. Study included T2DM patients (30 – 70 years age group). We excluded the patients with renal failure, who had acute myocardial infarction (MI) in last 6 months, with history of alcohol abuse, on Mg supplements or Mg containing antacids, with malabsorption and chronic diarrhea. The study population included 75 patients attending diabetic clinic as the main target group in the study. For correlating the study 40 control cases were included from outpatient wing of General Medicine. Ethical clearance for this study was obtained from Ethical Review Committee of Medical College Hospital, and informed consent of the patients was obtained before the study. Blood samples were collected for each patient to estimate serum urea, serum creatinine, fasting plasma glucose (FPG), post-prandial plasma glucose (PPG), serum magnesium, serum calcium and HbA1c levels. Analysis was done using SPSS software and Pearson's correlation was employed between the study variables to find the relationships.

RESULTS

In main target group 36% were at the age group of 41-50 years followed by 29.3% each at the age group of 51-60 years and 61-70 years. Only 5.3% were at the age group of 31-40 years. In this group 72% were females and 28% were males.

diabetic retinopathy, 2.6% had diabetic retinopathy and cellulitis and 2.6% had diabetic neuropathy. Moreover 14% of the total case had no complications (Table 2). About 37.3% had FPG in the range of 150-200 mg/dL, 33.3% cases reported FPG in the range of <150 mg/dL and 29.4% had FPG>200 mg/dL. In control group 47.5% had FPG <100 mg/dL, 32.5% had FPG in the range of 101-110 mg/dL and 20% had FPG in the range of 111-120 mg/dL. None of the controls had elevated FPG>120 mg/dL. About 34.7% had PPG in the range of 151-200 mg/dL, followed by 26.7% having PPG in the range of 201-250 mg/dL 20% had PPG at the range of 251-300 mg/dL and 18.7% had >300 mg/dL. In control group 50% had PPG in the range of 131-150 mg/dL, 25% had in the range of 121-130 mg/dL, 12.5% in the range of 101-110 mg/dL, 10% had in the range of 111-120 mg/dL. Only one patient from control group had PPG<100 mg/dL. About 69.3%, 18.7% and 12% diabetes cases reported HbA1c 7-9%, >9% and 6.5-7% respectively.

In main target group about 30.6% and 69.4% of patients had magnesium level <1.5 mg/dL and ≥1.5 mg/dL. All the control group patient reported to have magnesium level ≥1.5 mg/dL. About 31.5% of female patients and 28.6% of male patients had hypomagnesaemia. When we analysed the distribution of hypomagnesaemia in diabetes according to age, we noticed that 13.3% and 10.6% cases were from age group of 61-70 years and 51-60 years respectively. Applying Pearson's correlation revealed negative correlation between Mg and age with $r = -0.240$ and $p = 0.038$ (Figure 1). While analyzing the duration of diabetes in patients with hypomagnesaemia we noticed that 20% patients had diabetes for >7 years and 10.6% of patients had diabetes between 4 to 7 years. Pearson's correlation revealed negative correlation between Mg and onset of diabetes with $r = -0.409$ and $p = 0.001$ (Figure 2).

Table 1. Demographic characters of participants

Group	Age in years				Gender		Duration of diabetes (years)		
	31-40	41-50	51-60	61-70	Male	Female	<4	4-7	>7
Control	30%	30%	25%	15%	50%	50%	N/A		
Diabetes	5.3%	36%	29.3%	29.3%	28%	72%	30.6%	30.6%	38.8%

Table 2. Distribution according to descriptive clinical criteria of diabetes mellitus

Complication	Frequency	Percentage
Uncomplicated	11	14.6
Hypertension	30	40
Hypothyroidism	4	5.3
Hypertension + hypothyroidism	4	5.3
Hypertension + cellulitis	13	17.3
Hypertension + diabetic neuropathy	5	6.6
Diabetic retinopathy + cellulitis	2	2.6
Hypertension + diabetic retinopathy	4	5.3
Diabetic neuropathy	2	2.6

In control group 30% each were at the age group of 31-40 years and 41-50 years followed by 25% at the age group of 51-60 years. In this group 50% each were males and females. We analyzed duration of diabetes in main target group where we found that 38.8% had diabetes for >7 years and 30.6% had diabetes for 4-7 years and the same percentage repeated in <4 years also (Table 1). Many of the patients had co-morbid conditions such as 40% patients had hypertension, 17.3% had both hypertension and cellulitis, 6.6% had both hypertension and diabetic neuropathy, 5.3% had hypothyroidism, 5.3% had hypertension and hypothyroidism, 5.3% had hypertension and

We also found moderate significant negative correlation between Mg and HbA1C with $r = -0.780$ and $p = 0.001$ (Figure 3), significant negative correlation between Mg and PPBS with $r = -0.706$ and $p = 0.001$ (Figure 4), and moderate significant negative correlation between Mg and FBS with $r = -0.733$ and $p = 0.001$ (Figure 5). We evaluated the relation between hypomagnesaemia and diabetes complications where we found that 43.5%, 30.4%, 21.6% and 8.7% of T2DM patients with hypomagnesaemia had cellulitis, diabetic neuropathy, diabetic retinopathy and mixed complications respectively. Also we evaluated the relation between hypomagnesaemia and

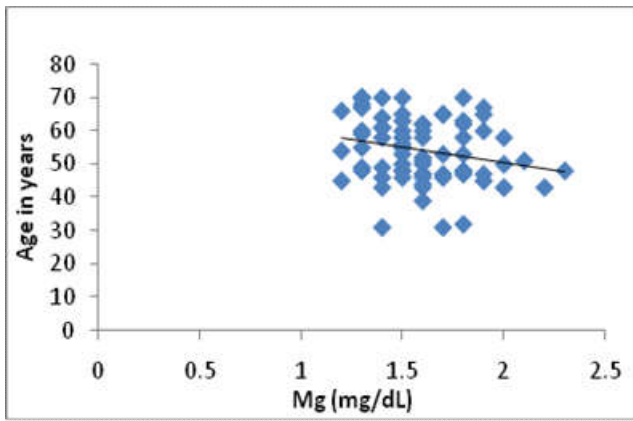


Figure 1. Correlation of Mg with Age

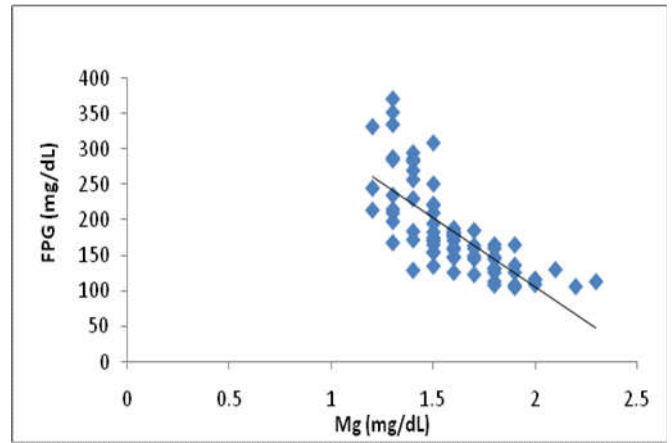


Figure 5. Correlation of Mg with FPG

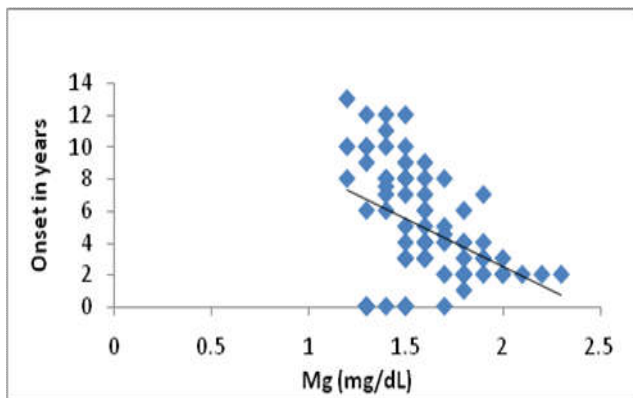


Figure 2. Correlation of Mg with onset of diabetes

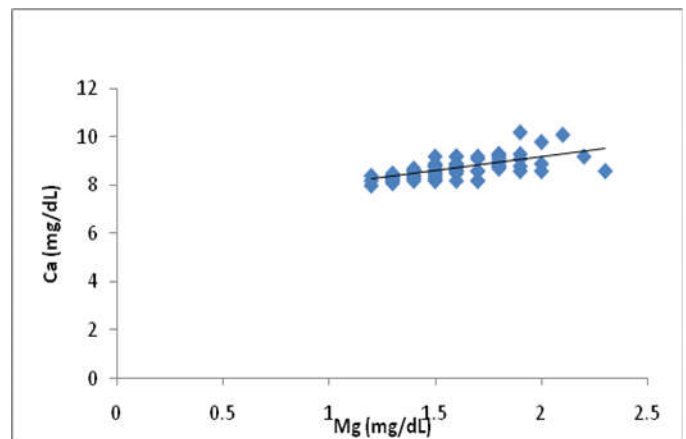


Figure 6. Correlation of Mg with Ca

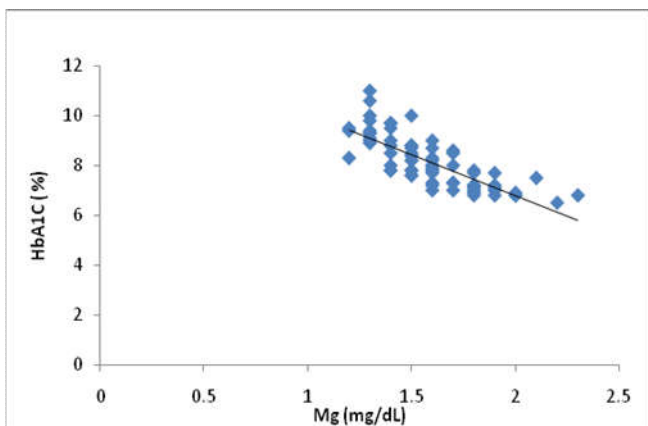


Figure 3. Correlation of Mg with HbA1C

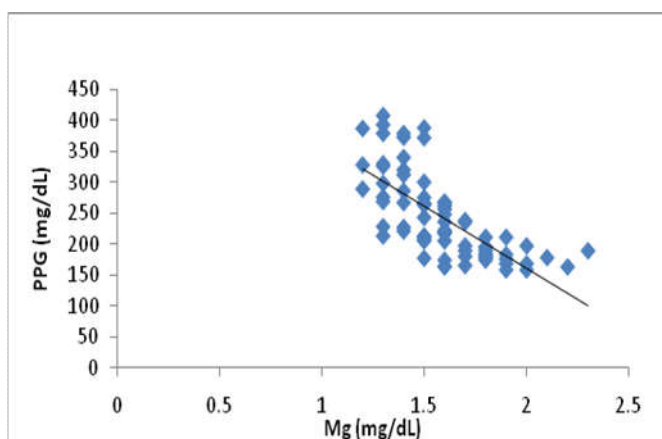


Figure 4. Correlation of Mg with PPG

hypocalcemia. Pearson correlation suggested moderate significant positive correlation between Mg and Ca with $r = 0.647$ and $p = 0.001$. About 29.3% of patients from main group had Ca level < 8.5 mg/dL and 70.7% patients had Ca level ≥ 8.5 mg/dL (Figure 6).

DISCUSSION

Diabetes Mellitus is one of the most common metabolic disorder and leading cause of death & disability in the world (International Diabetes Federation, 2015 and Praveena *et al.*, 2013). It is due to absolute or relative insulin deficiency. Many trace elements are important for human metabolic function. Numerous studies have demonstrated the essential roles of trace elements as magnesium, calcium, chromium, zinc, selenium, vanadium, molybdenum and manganese in insulin action and carbohydrate metabolism (Praveena *et al.*, 2013). The current study population included age matched 115 patients i.e., 75 cases who attended the Diabetic clinic and 40 controls who attended the out- patient wing of General Medicine during the study period. In main target group 72% were females and 28% were males. In control group 50% were females and 50% were males. Most of the studies preferred the similar age group but did not excluded renal complicated cases. In our study excluded renal complicated cases. The present study showed a suggestive negative correlation between serum Mg and age with $r = -0.240$, $p = 0.038$ which was similar to the finding of Nasri *et al* but with $r = -0.775$. Moreover In the study conducted by Mishra *et al.*, showed a negative correlation between serum Mg and duration of diabetes, in the current study also similar result was obtained with $r = -0.409$ and $p = 0.001$ (Mishra *et al.* 2012).

We evaluated the relation between hypomagnesemia and diabetes complications where we found that 43.5%, 30.4%, 21.6% and 8.7% of T2DM patients with hypomagnesemia had cellulitis, diabetic neuropathy, diabetic retinopathy and mixed complications respectively. We analyzed the correlation between Mg and glucose parameters where we found significant netagive correlation between Mg and HbA1c ($r = -0.780$ and $p = 0.001$), and Mg and PPBS ($r = -0.706$ and $p = 0.001$). But the correlation between Mg and FBS reported moderate significant negative correlation ($r = -0.733$ and $p = 0.001$). Similarly study done by Ahmed MM *et al* reported negative correlation, with $r = -0.621$ and $p = 0.05$, between Mg and HbA1c (Ahmed *et al.*, 2002). Study demonstrated by Tripathy S, *et al.* also showed a significant negative correlation between serum Mg and glucose levels (Tripathy *et al.*, 2004), and study conducted by Mishra *et al.*, also reported a significant negative correlation between serum Mg and FBS (Mishra *et al.*, 2012).

Conclusion

The study revealed

- Low magnesium status is common in type 2 Diabetes Mellitus patients when compared to non diabetes controls
- Hypomagnesaemia is associated with micro vascular complications and poor glycemic control
- Supplementing magnesium may have beneficial role in Diabetes Mellitus
- It is important to periodically monitor magnesium levels in all type 2 diabetes patients

Further studies on the role of magnesium supplementation in Type 2 Diabetes Mellitus are necessary.

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