

Serum Magnesium Level in Type 2 Diabetes Mellitus and its Relationship with Glycemic Control and Diabetic Complications

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Abstract

Introduction: Diabetes is frequently associated with Mg deficit. The most but not all diabetic subjects have low magnesium (Mg). Hypomagnesaemia has been reported to occur in 25-38% of patients with Type 2 DM especially in those without good metabolic control. Deficiency of Mg may increase the incidence of diabetes mellitus (DM) and occurrence of diabetic complications. It is frequently overlooked and undertreated. A low Mg intake and an increased Mg urinary loss appear to be the most important mechanisms that may favor Mg depletion in patients with type 2 diabetes.

Objectives: The present study was conducted with an objective to evaluate the serum magnesium level in type 2 Diabetes mellitus. The present study also attempts to evaluate an association between the serum magnesium levels with duration of diabetes, glycosylated hemoglobin and diabetic complications.

Methods and Materials: This is a cross sectional study which was done between July 2016 to August 2017 in Khaja Banda Institute of Medical College and Hospital. A total of 100 Type 2 DM patients were included in the study. The serum blood sugar level, HbA1C (%), magnesium level was estimated and the serum magnesium levels were correlated with the duration of diabetes, glycosylated hemoglobin and diabetic complications.

Results: Among the 100 patients, 58% were men and 42% were women. Mean age was 56.98±8.76 years and the mean duration of diabetes were 8.2±4.8 years. The mean glycosylated hemoglobin (HbA1c) was 7.44±1.43%. The mean serum magnesium was 1.78±0.48 mg/dl. Out of 100 patients, 66 patients had normal serum magnesium levels and 34 patients had hypomagnesaemia. There was no correlation between serum magnesium levels with increasing duration of diabetes. Out of the 34 patients who had hypomagnesaemia, 29 patients had HbA1c > 7%. This correlated between hypomagnesaemia and poor glycemic control in our study. There were 16 patients who had retinopathy, 20 patients had nephropathy and 26 patients had neuropathy. Among the 34 patients, 24 had complications and 10 patients did not have any complications. However there was a weak negative correlation between serum Mg levels ($r = -0.110$, $p = 0.004$) and diabetic complications.

Conclusion: Serum magnesium level was low in most of the Type 2 DM patients with poor glycemic control. Mg depletion affects both glycemic regulation and the occurrence of complications. Also, poor glycemic regulation affects serum Mg levels.

Keywords: Type 2 Diabetes Mellitus; Glycemic Control; Serum Magnesium.

Introduction

Type 2 diabetes mellitus is most prevalent among worldwide. It is a metabolic and endocrinological

disease characterized by hyperglycemia associated with insulin resistance or decreased insulin secretion [1]. The prevalence of diabetes was around 4% worldwide [2]. The Type 2 diabetes

mellitus patients may have cardiovascular disease, nephropathy, retinopathy and polyneuropathy [3]. The recent WHO report suggests that over 19% of worlds diabetic population currently resides in India [2].

Magnesium (Mg) deficiency is a common problem in diabetic patients. Magnesium is an electrolyte, which has a critical role in the enzymatic reactions and is the fourth most abundant cation in the human body [4]. It is also an essential enzyme activator for neuromuscular excitability and cell permeability, a regulator of ion channels and mitochondrial function, a critical element in cellular proliferation and apoptosis, and an important factor in both cellular and humoral functions [5]. Hypomagnesaemia has been reported to occur in 25-38% of patients with type 2DM especially in those without good control [6]. Its deficiency may increase insulin resistance. The reasons for magnesium deficiency in diabetes are not very clear. This could be due to higher urinary loss and lower dietary intake/impaired absorption [7]. Serum magnesium levels have wide ranging impact on diabetic control and complications [8]. An increased prevalence of Mg deficits has been identified in those with poorly controlled glycemic profiles, with longer duration of the disease and with the presence of micro and macro vascular chronic complications [9,10]. This present study had been undertaken to estimate the serum magnesium levels in type 2 DM patients and its relation with glycemic control, duration of diabetes and its complications.

Materials and Methods

This cross sectional study had been done over a period of one year from April 2016 to March 2017 on 100 patients attending KBN Teaching and General Hospital as both outpatients and inpatients. The patients with type 2DM above the age of 40 years were included in this study. Patients with type 1 DM, acute or chronic diarrhea, history of alcohol intake, malabsorption syndrome and those on mineral supplementation, thyroid or adrenal dysfunction, on diuretics and adverse renal function were excluded from the study.

The diagnosis of type 2 DM was confirmed by biochemical investigations as per WHO criteria [11]. Detailed history was taken and examination was done to diagnose micro vascular and macro vascular complications of Diabetes. Diagnosis of diabetic neuropathy was confirmed by a detailed medical history and neurological examination. Diabetic retinopathy was diagnosed

with fundus examination. Diabetic nephropathy was diagnosed by ultrasound scanning. Serum Mg levels were estimated by specific electrode ionic method. The serum magnesium level between 1.5-2.5 mg/dl was taken as normal. Patients were considered frankly hypomagnesaemia when serum Mg concentrations are < 1.5mg/dl.

Results

A cross sectional study consisting of 100 Type 2 DM patients had been done to know the serum magnesium level and its relation with duration of diabetes, glycosylated hemoglobin and diabetic complications. The mean age of the diabetics was 56.98±8.76 years. Out of 100 patients, 58 patients were males and 42 patients were females. The maximum number of patients was found between the age groups 50 to 60 years of age. The mean magnesium level was 1.78±0.48 mg. The serum magnesium levels were low in 34 patients and were normal in 66 patients [Table 1].

The duration of diabetes was less than 5 years in 44 patients, 5 to 10 years in 30 patients and more than 10 years in 26 patients. The mean serum magnesium level in 5 years, 5 to 10 years and more than 10 years patients were 1.67±0.42 mg, 1.99±0.51 mg and 1.74±0.55 mg respectively. Out of 34 patients with low magnesium level, 16 (47%) patients had less than 5 years duration, 09 (26.5%) patients had 5 to 10 years duration and 09 (26.5%) patients had more than 10 years duration. So there was no correlation of serum magnesium level with duration of diabetes mellitus. The p value was >0.001 and r value 0.085 [Table 2].

The mean HbA1c level was 5.54±0.26 in 21 patients with mean magnesium level 2.21±0.43 mg, 18 patients had mean HbA1c level of 6.63±0.29 with mean magnesium level 1.95±0.50 mg, 32 patients had mean HbA1c level of 7.50±0.20 with mean magnesium level 1.72±0.36 mg, 19 patients had mean HbA1c level of 8.53±0.25 with mean magnesium level 1.50±0.31 mg, 06 patients had mean HbA1c level of 9.58±0.28 with mean magnesium level 1.43±0.43 mg and 4 patients had mean HbA1c level of 11.20±0.70 with mean magnesium level 1.23±0.36mg [Table 3]. Out of 21 patients with mean HbA1c 5.54±0.26, no one had low serum Mg level, 18 patients with mean HbA1c 6.63±0.29, 5 (27.8%) patients had low Mg level, 32 patients with mean HbA1c 7.50±0.20, 11(34.4%) had low Mg level, 19 patients with mean HbA1c 8.53±0.25, 11 (57.9%) had low Mg level, 6 patients with mean HbA1c 9.58±0.28, 4 (66.7%) had low Mg level and 4 patients

with mean HbA1c 11.20±0.70, 3 (75%) had low Mg level [Table 4 & 5]. Out of 34 patients with low serum Mg level, 29 (85.3%) patients had HbA1c level more than 7.0%. The magnesium levels were low in those patients who had high HbA1c levels and were normal in those patients who had controlled HbA1c levels. There was a significant negative correlation between HbA1c and serum magnesium levels with p value <0.001 [Table 3 & 4].

Out of 100 patients, 62 patients had one or more micro vascular complications and 38 patients had no complications. Of the 62 patients with diabetic complications, 24 (38.7%) patients had low magnesium levels and 38 (61.3%) patients had normal magnesium levels. Of the 38 patients who had no complications, 28 (73.7%) patients had normal magnesium levels and 10 (26.3%) patients had low magnesium levels. The magnesium level was low in more number of patients who had complications than those who did not have complications. The mean magnesium level of patients with diabetic complications was 1.65±0.37 mg and without complications was 1.84±0.54 mg [Table 5 & 6]. This difference was significant as the p value was >0.05 (p-value 0.048).

Of these 62 patients with diabetic complications, 16 (25.8%) patients had retinopathy, 20 (32.3%) patients had nephropathy and 26 (41.9%) patients had neuropathy. The mean magnesium level in retinopathy, neuropathy and nephropathy patients was 1.76±0.41 mg, 1.57±0.34 mg and 1.62±0.38 mg respectively. The correlation was analyzed but there was no correlation between serum magnesium level and diabetic complications with chi square value 1.89 and p value 0.389 which is not significant (p>0.01).

Table 1: Serum Magnesium level

Serum Mg level (mg)	No. of patients	Percentage (%)
<1.5	34	34
1.5-2.0	46	46
2.1-2.5	12	12
>2.5	08	08
Total	100	100

Table 2: Correlation of serum Magnesium level with duration of diabetes

Duration of Diabetes	Serum Mg level (mg)	Total no. of patients	Percentage (%)
<5 yrs	1.67±0.42	44	44
5-10 yrs	1.99±0.51	30	30
>10 yrs	1.74±0.55	26	26

Table 3: Distribution of patients according to HbA1C with serum Mg level

Serum Mg level	<6	6.1-7.0	7.1-8.0	8.1-9.0	9.1-10	>10	No. of Patients
<1.5	00	05	11	11	04	03	34
1.5- 1.9	11	06	17	08	02	01	45
2.0-2.5	06	04	02	00	00	00	12
>2.5	04	03	02	00	00	00	09
Total	21	18	32	19	06	04	100

Table 4: Correlation of HbA_{1c} with serum Mg level

Mean HbA1C level	Mean serum Mg level	No. of patients	Percentage (%)
5.54±0.26	2.21±0.43	21	21
6.63±0.29	1.95±0.50	18	18
7.50±0.20	1.72±0.36	32	32
8.53±0.25	1.50±0.31	19	19
9.58±0.28	1.43±0.43	06	06
11.20±0.70	1.23±0.36	04	04

Table 5: Relation of Hypomagnesaemia with diabetic complications

Mean of Mg level with complications	No. of patients	Mean of Mg level without complications	No. of patients
1.65±0.37	62	1.84±0.54	38

Table 6: Relation of serum Mg level with micro vascular complications

Complications	Low Mg level(mg)	Normal Mg level(mg)	Mean± SD
Retinopathy	04	12	1.76±0.41
Neuropathy	12	14	1.57±0.34
Nephropathy	08	12	1.62±0.38

Discussion

Diabetes mellitus is the most common endocrine disorder associated with low serum magnesium level. Intracellular Mg plays a role in regulating insulin action, insulin dependent glucose intake and vascular tone. Deficiency of cellular Mg can reduce tyrosine kinase activity, post receptorial activity and eventually it may contribute to the development of insulin resistance [12]. The possible link between Mg deficiency and reduced insulin sensitivity is the presence of oxidative stress and/or inflammation. Thus, free radicals are often increased in type 2 DM, hypertension, metabolic syndrome and aging conditions which are also associated with Mg deficits [13].

Hypomagnesaemia has been reported to occur in 25-38% of patients with type 2DM especially in

those without good blood sugar control [6]. A. G. Kulkarni et al and Mohamed Murtuza Kauser et al. in their study concluded that serum magnesium level was lower in most of Type 2 DM [14,15]. In our study out of 100 patients 34 patients had decrease in serum magnesium level. Similar such decreased in serum magnesium level in diabetic patients as compared to controls has been reported in other studies [16,17].

An increased prevalence of Mg deficits has been identified in those with longer duration of the disease [9,10]. But a study by AH Zagar, NA Shah et al did not show the any influence of duration of diabetes on magnesium concentrations [18]. In our study, the mean magnesium level was lower in patients with less than 5 years of duration and was high in those with 5-10 years duration. The patients with more than 10 years duration had mean magnesium level more than those with less than 5 years duration. There was no decrease in magnesium level as the duration increased. So there was no correlation between serum magnesium level and duration of diabetes mellitus.

Poor glycemic control in diabetic patients is a well-known risk factor for Mg depletion in diabetic patients [19]. Significant negative correlation between Mg and HbA1c had been found in some of the studies [20,21]. Similarly, we found a negative correlation between serum Mg level and HbA1c level. Out of the 34 patients who had hypomagnesaemia, 29 patients had HbA1c > 7%. This correlation between hypomagnesaemia and poor glycemic control was statically significant ($p < 0.001$). Similarly S. Ramadass et al. in his study found serum magnesium levels decline with rise in HbA1c levels in Type 2 DM [9]. Sharma A et al. in his study concluded poor glycemic control was associated with hypomagnesaemia [22]. But Zurich, Switzerland, Walti MK et al. in their study found that hypomagnesaemia was common in Type 2 DM but did not have any significant correlation with HbA1c [23].

Mg deficiency may be also a factor implicated in DM2 complications. It can potentiate chronic diabetic complications probably as a result of its positive action in inositol transport (through ATPase activation) [24] or its action of reducing platelet aggregation. Hypomagnesaemia leads to rapid decline in kidney function and thus it is currently considered as an accurate predictor of progression of diabetic nephropathy [25,26]. Hypomagnesaemia may be a contributing factor for the long term complications particularly ischemic heart disease, retinopathy [27,28], foot ulcer and peripheral neuropathy [6].

In the present study, 62 patients had micro vascular complications and 38 patients had no complications. Of the 62 patients with diabetic complications, 24 (38.7%) patients had low magnesium levels and 38 (61.3%) patients had normal magnesium levels. Of the 38 patients who had no complications, 28 (73.7%) patients had normal magnesium levels and 10 (26.3%) patients had low magnesium levels. The magnesium level was low in more number of patients who had complications than those who did not have complications. The mean magnesium level of patients with diabetic complications was 1.65 ± 0.37 mg and without complications was 1.84 ± 0.54 mg. This difference was significant as the p-value was > 0.05 . But there was no correlation with serum magnesium level and diabetic complications as 38 patients who had normal serum magnesium level also had diabetic complications and only 24 patients with low serum magnesium level had diabetic complications. These results were probably because of dyslipidemia and uncontrolled glycosylated hemoglobin levels which are responsible for micro- and macro vascular complications in diabetes along with hypomagnesaemia as they lead to higher degree of atherosclerosis.

Conclusion

Hypomagnesaemia is present in most of the patients with type 2 diabetes. Contributory mechanisms most likely are multifactorial. It has been found to be associated with poor glycemic control. Diabetic complications were more common in patients with hypomagnesaemia. Since most but not all type 2 diabetics have low serum magnesium level, supplementation with magnesium in addition to classical therapies for diabetes may help in prevention or delaying of diabetic complication. Further, large studies are required to support the role of magnesium supplementation in type 2 DM.

Limitations

The study population is limited. It requires a large study population and elaborate study to know the relation of serum magnesium level and other trace elements with Type 2 DM.

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