FREQUENCY OF HYPOMAGNESEMIA IN PATIENTS WITH UNCONTROLLED TYPE II DIABETES MELLITUS

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ABSTRACT

Objective: The objective of this study was to determine the frequency of Hypomagnesemia in patients with uncontrolled type II diabetes mellitus.

Study Design: Cross-sectional study.

Place and Duration of Study: Department of Medicine, PNS Shifa Naval Hospital Karachi, from Jul 2012 to Dec 2012 over a period of six months.

Material and Methods: In this study, three hundred and twenty three patients of uncontrolled diabetes mellitus type-II on oral hypoglycemic agents for more than five years, presenting to medical OPD, were recruited. All patients fulfilled inclusion and exclusion criteria. Blood samples of all patients for serum HbA1c and serum magnesium levels were analyzed at the time of enrollment. Statistical analysis was done on SPSS 20.

Results: Out of 323 patients, 243 (75.23%) were males and 80 (24.76%) were females with the age ranging from 40 – 65 years (mean age and SD 54.76 ± 6.43). Hypomagnesemia was found in 117 patients, without any significant difference in men and women (38.45% and 35.39% respectively). The mean duration of diabetes was 12.5 years (ranging from 5 to 22 years). By frequency test in SPSS-20, the highest frequency of hypomagnesemia (49.42%) is seen in (8.6–9.0) HbA1c group while lowest frequency hypomagnesemia (15.38%) is seen in (>10.0) HbA1c level group mean standard deviation and *p*-value calculated by Pearson correlation statistic in SPSS-20 for quantitative variables (HbA1c, Magnesium level).

Conclusion: Hypomagnesemia is frequent in poorly controlled type-II diabetes mellitus having increased level of HbA1c. So it may be prudent in clinical practice to periodically monitor plasma magnesium and HbA1c in type-II diabetes mellitus patients.

Keywords: HbA1c, Magnesium, Type II diabetes mellitus.

INTRODUCTION

Diabetes is a disorder resulting from insufficient production and / or inefficient use of insulin. Magnesium (Mg) is the second most important intracellular cation and is a cofactor in both glucose transporting mechanism of cell membranes and various enzymes important in carbohydrate oxidation[1]. Hypomagnesemia is a commonly overlooked electrolyte abnormality in hospitalized patients having type-II diabetes mellitus[2]. Hypomagnesemia has been reported in 13.5 to 47.7% of non-hospitalized patients with type-II diabetes as compared to 2.5 to 15% hospitalized patients without diabetes[3]. Clinically, there are significant data linking hypomagnesemia to various micro and macro vascular complications of diabetes[4,5]. In patients with diabetes mellitus, hypomagnesemia has been linked to poor glycemic control, and increased risk of coronary artery disease, hypertension, diabetic retinopathy, nephropathy, neuropathy, and foot ulcerations[6]. It has been suggested that daily magnesium replacement in such patients can improve the glycemic control and reduce the progression and severity of diabetic complications[7].

The disturbance in serum magnesium level i.e. hypomagnesemia has been reported to occur among patients of diabetes mellitus[8].

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The prevalence of hypomagnesemia in diabetes mellitus is 65%[9]. The persistent hypomagnesemia leads to raised serum glucose level, insulin resistance and the degree of magnesium depletion correlates positively with serum glucose concentration and the degree of glycosuria[10]. Glycosylated HbA1c level of more than 7.5% was considered as raised, and reflects poor glycemic control and was noted in 42% of type-II diabetic patients[11,12]. Intracellular Mg plays a key role in regulating insulin action, insulin-mediated-glucose uptake and vascular tone. Reduced intracellular magnesium concentrations result in a defective tyrosine-kinase activity, post-receptorial impairment in insulin action and worsening of insulin resistance in diabetic patients.

In the presence of diabetes, it is observed that inadequate metabolic control can affect the concentrations of magnesium, hypomagnesemia, which may be still directly related with some micro and macro vascular complications observed in diabetes as cardiovascular disease, retinopathy and neuropathy[13]. Some epidemiologic studies have indicated that the mortality from ischemic heart disease (IHD) is lower in populations living in areas with "hard" water (i.e. water with high calcium and magnesium concentrations) than in populations living in areas with water having low concentrations of these minerals. Hypomagnesemia is also reported in 47.7% of non-hospitalized patients with uncontrolled type-II diabetes mellitus having some degree of chronic kidney disease[14]. There is considerable evidence to suggest that hypomagnesemia may adversely affect various aspects of cellular physiology. Available data suggest that low magnesium levels may promote endothelial cell dysfunction and greater tendency of thrombogenesis by increasing platelet aggregation and vascular calcifications[14]. Hyperglycemia is inversely related to hypomagnesemia and serum magnesium can be used for prognostic assessment in diabetic individuals.

Keeping in view the evidence linking hypomagnesemia with uncontrolled type-II diabetes mellitus, limited locally available data and enormous burden of diabetics in our population, it was planned to measure the frequency of hypomagnesemia in subjects who demonstrated poor glycemic control evident with raised HbA1c.

MATERIAL AND METHODS

This cross-sectional study was conducted at PNS Shifa Naval Hospital, Karachi from July 2012 to December 2012 over a period of six months after seeking approval from hospital ethical committee. All patients were aged between 40– 65 years. They were known cases of diabetes mellitus type-II with persistently raised HbA1c of more than 7.5% and taking oral hypoglycemic agents for more than five years. Exclusion criteria included type-I

Table-I: Frequency of hypomagnesaemia with gender specification.

Gender	No. of pateints	Patients with hypomagnesemia	Frequency (%)
Male	243	86	35.39
Female	80	31	38.75
Total	323	117	36.22

Table-II: Mean and std deviation of hypomagnesaemia, normomagnesaemia group statistics.

Magnesium	N	Mean	Std. Deviation	Std. Error Mean
Normomagnesemia	206	3.54	1.402	.098
Hypomagnesemia	117	3.64	1.054	.097

Table-III: Mean and std deviation of HbA1c and magnesium level.

	Descriptive statistics		
	Mean	Std. Deviation	N
HbA1c	3.58	1.286	323
Magnesium	1.36	.481	323

diabetes mellitus, secondary causes of diabetes mellitus (like haemochromatosis, Cushing's disease, acromegaly), chronic diarrhea, hypo-proteinemic states (like chronic liver disease) and controlled diabetes mellitus type II with HbA1c less than 7.5%. Three hundred and twenty three patients of uncontrolled diabetes mellitus type-II on oral hypoglycemic for more than five years, presenting to medical OPD were selected by consecutive non-probability sampling technique after getting informed consent. All patients were interviewed, examined in details and pertinent aspects of patients' data were recorded. Venous blood samples were collected at OPD using full aseptic measures and immediately transported to pathology department, PNS Shifa hospital in closed bottles held in vertical position. Serum HbA1c and serum magnesium levels were analyzed by calmagite dye method using auto analyzer, under supervision of chemical pathologist and results were entered in a designated proforma.

Patients with serum magnesium less than 0.6 mmol/l were labeled as having hypomagnesemia and serum magnesium level 0.6 mmol/l and more were having normomagnesemia.

All data collected were entered in SPSS version 20.0. Mean and standard deviation (Mean ± SD) were calculated for quantitative variables like age of patient, duration of diabetes, serum magnesium levels, fasting blood glucose, random blood glucose and glycosylated hemoglobin (HbA1c). Frequency and percentages were presented for qualitative variables i.e. gender and serum magnesium levels (outcome). Frequency is calculated by frequency test in descriptive statistic. Mean and SD is calculated by group statistic, *p*-value is calculated by Pearson correlation statistic in SPSS-20.

RESULTS

In our study, a total of 323 patients were selected. Of those, 243 (75.23%) were males and 80 (24.76%) were females. The age among all subjects ranged from 40–65 years (mean age and SD 54.76 ± 6.43). Most patients (n=93) were in age group of 46 – 50 years of age.

Hypomagnesemia (serum magnesium <0.6 mmol/l) was found in 117/323 (36.21%) patients whereas 206/323 (63.77%) had normal magnesium levels. Frequency/ percentage was calculated by frequency test in descriptive statistic spss-20 shown in (table-I) (fig-1).

Mean and std deviation of HbA1c and magnesium level is calculated by descriptive statistics in SPSS-20, shown in (table-II, III)

Mean duration of diabetes mellitus type-II was 12.5 years (range 5–22 years). *p*-value 0.57 by

Table-IV: Frequency of Hypomagnesaemia with HbA1c.

HbA1c	No of pateints	Hypomagnesemia	Frequency (%)
7.5-8.0	28	5	17.85
8.1-8.5	32	6	18.75
8.6-9.0	87	43	49.42
9.1-9.5	91	37	40.65
9.6-10.0	72	24	33.33
>10.0	13	2	15.38

Table-V: Magnesium Level (mmol/L) in relation to HbA1c.

HbA1c	Magnesium level (mmol/L)			Total	Frequency (%)
	0.5	0.4	0.3		
7.5-8.0	03	01	01	5	17.85
8.1-8.5	05	01	00	6	18.75
8.6-9.0	19	22	02	43	49.42
9.1-9.5	26	09	02	37	40.65
9.6-10.0	15	08	01	24	33.33
>10.0	02	00	00	2	15.38

correlation descriptive statistic in SPSS-20 and 0.05 was taken as significant. So the duration of diabetes did not significantly predict serum magnesium concentrations.

Frequency of hypomagnesemia with HbA1c is calculated by frequency test in descriptive statistics is shown in (table-IV, V). Association of Hypomagnesemia with HbA1c is calculated by Pearson correlation statistic is shown in (table-IV-V), *p*-value 0.493, so the correlation is insignificant at *p*-value more than 0.05.

DISCUSSION

In diabetes mellitus type-II, it is observed that inadequate metabolic control can affect the concentrations of magnesium, developing hypomagnesemia, which may be directly related with some micro and macro vascular complications observed in diabetics as cardiovascular events, retinopathy and neuropathy[13-15]. In this study, serum magnesium concentrations of 117 patients (34.11%) with type-II diabetes were below the reference range. This confirms the reported prevalence of low plasma magnesium status in type-II diabetics in several studies, which ranged from 25 to 39%. Prevalence of hypomagnesemia in type-II diabetics in our study was similar to that reported by Nadler et al[16] in type-II diabetics, attending outpatient clinics in the US. Walti MK et al[17] also reported a prevalence of hypomagnesemia in type-II diabetics at 37.6% versus 10.9% in non-diabetic controls in a study conducted in Zurich, Switzerland.

The reasons for the high prevalence of magnesium deficiency in diabetes are not clear, but may include increased urinary loss, lower dietary intake, or impaired absorption of magnesium compared to healthy individuals. Several studies have reported increased urinary magnesium excretion in type-I & II diabetes[18]. A dietary assessment conducted in 97 type-II diabetics and 100 healthy controls showed that only 5.4% of the diabetic group and 9.1% of the control group were predicted to have intakes of magnesium below their individual requirements[19]. In addition, we have recently shown that type-II diabetics in reasonable metabolic control and without nephropathy absorb dietary magnesium to a similar extent as healthy controls, and have similar rates of urinary excretion[20]. Increased urinary magnesium excretion due to hyperglycemia and osmotic diuresis may contribute to hypomagnesemia in diabetes[18].

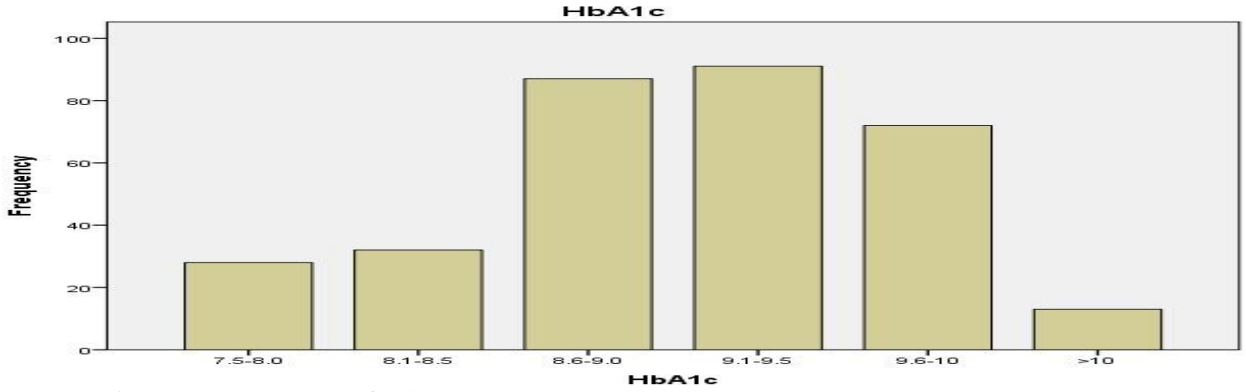

Figure: Frequency of HbA1c.

Serum levels of magnesium have been found by several investigators to correlate inversely with fasting blood glucose concentration[21,22] and the percentage of HbA1c[21]. In our study hypomagnesemia is observed in patients with poor glycemic control evaluated by estimation of HbA1c, the present study confirms the previous report by Schlienger et al[23] who studied the influence of glycemic control (glycemic control evaluated by HbA1c) on various trace elements and reported significantly reduced plasma magnesium levels in patients with poor control of

diabetes. Furthermore present study is also in conjunction with study by Shaikh MK et al[20,11,24].

Glycosylated hemoglobin (HbA1c) results from glycosylation of hemoglobin by a reaction between glucose and N-terminal valine of beta chain of Hb molecules. When plasma glucose is consistently elevated, there is an increased glycosylation of hemoglobin. HbA1c assays approximate with mean plasma glucose values over previous 2 to 3 months. Higher percentages of HbA1c indicate poor glycemic control in the previous months.

Hypomagnesemia is reported to be both a cause and result of poor glycemic control. Magnesium is a cofactor in both glucose transporting mechanisms of cell membrane and various enzymes important in carbohydrate oxidation[25]. In addition, magnesium deficiency has been shown to promote insulin resistance in multiple studies. Nadler et al[26] have reported that insulin sensitivity decreases even in non-diabetic individuals after induction of magnesium deficiency. Likewise, elderly subjects were shown to have improved glucose tolerance when they received magnesium supplements. Thus hypomagnesemia by itself results in poor glycemic control. Conversely, hyperglycemia and osmotic diuresis may lead to increased urinary magnesium excretion and hypomagnesemia in diabetics. However, high prevalence of hypomagnesemia is reported in type-II diabetics with good glycemic control[16]. So, although poor glycemic control is associated with magnesium deficiency, it is not simply induced by hyperglycemia and is not corrected by improvement in metabolic control alone.

Sex, age and duration of diabetes were not the significant predictors of serum magnesium levels. Yajnick et al reported that among diabetics plasma magnesium concentration was directly related to age and men had significantly higher concentrations than women. The increasing magnesium levels with age were probably due to impaired renal function was relatively small to confirm male preponderance. In our study, patients with impaired renal functions were excluded. Our results confirm to the recent reports that have not shown any significant associations between sex, age and duration of diabetes with serum magnesium levels[17].

CONCLUSION

Hypomagnesaemia is common in type-II diabetes mellitus and magnesium deficiency is conclusively associated with increased level of HbA1c. So it may be prudent in clinical practice to periodically monitor plasma magnesium and HbA1c in type-II diabetes mellitus patients.

CONFLICT OF INTEREST

This study has no conflict of interest to declare by any author.

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