Original Article

Hypomagnesaemia among patients with type 2 diabetes mellitus and impaired glucose tolerance and its correlation with glycemic control: a cross-sectional study in a tertiary care hospital of Bangladesh

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ABSTRACT

Background: *Hypomagnesaemia is linked to insulin resistance in type 2 diabetes mellitus (T2DM) and chronic diabetic complications. Prevalence of hypomagnesaemia is high in patients with T2DM and multiple studies have shown evidence of effect of serum magnesium (Mg) level on glycaemic control in these patients. The aims of this study were to evaluate the frequency of hypomagnesaemia in hospitalized patients with T2DM and impaired glucose tolerance (IGT) and to evaluate its correlation with glycaemic control.*

Methods: *This was a cross-sectional study conducted from November, 2016 to March, 2017 in BIRDEM General Hospital. Hypomagnesaemia was defined as serum Mg concentration <0.7 mmol/L. Patients who had acute diarrhea or vomiting in previous 7 days, patients who had chronic diarrhea or malabsorpsion syndrome or who had recent history of taking diuretics were excluded from the study. Patients' clinical information were collected using a structured questionnaire and laboratory information were collected from the hospital records.*

Results: *Total patients were 100, including T2DM (92) and IGT (8). Thirty nine (42.4%) patients with T2DM and five (62.5%) patients with IGT had hypomagnesaemia. The median (IQR) serum Mg level in patients with T2DM was 0.77 (0.6-0.8) mmol/L and IGT was 0.6 (0.52-0.77) mmol/L. HbA1c was higher among patients with hypomagnesaemia than normal Mg level [median (IQR) 9.4 (7.8-12.7) % vs 8.85 (7.2-9.95) %] though it was not significant (p>0.05). The mean fasting blood glucose (FBG) was 9.82 mmol/l in patients with hypomagnesaemia and 9.63 mmol/l in patients with normal serum Mg. Median 2-hour post prandial blood glucose level was 12 (10.4-16.15) mmol/L in hypomagnesaemia group and 11.7 (10.3-14.7) mmol/L in normal Mg group, though the difference was not statistically significant. There was negative correlation between serum Mg and HbA1c, FBG and post prandial blood glucose level (r, -0.075, -0.003. -0.006 respectively). Among the patients with hypomagnesaemia, the percentage of ischemic heart disease (IHD), diabetic retinopathy, diabetic nephropathy and diabetic neuropathy was 31.8%, 36.4%, 43.2% and 34.1% compared to 23.2%, 30.4%, 32.1% and 25% respectively in patients with normal Mg level.*

Conclusion: *Around half of the patients with T2DM and IGT had hypomagnesaemia and patients with hypomagnesaemia were found to have relatively poor glycemic control and had increased rate of diabetic complications. Although relationship between serum magnesium level and glycemic control was not significant, it indicated the need of further research in this aspect.*

Key words: *hypomagnesemia, type 2 diabetes mellitus, impaired glucose tolerance.*

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INTRODUCTION

Globally, over 300 million people suffer from type 2 diabetes mellitus (T2DM).[1] T2DM is characterized by combination of insulin deficiency and insulin resistance. Magnesium is an essential ion in human which is involved in various functions including energy homeostasis, protein synthesis, DNA stability.[2] In healthy individual, serum magnesium is regulated between 0.7-1.05 mmol/L.[2] Magnesium is associated with glucose metabolism, insulin secretion and insulin sensitivity.[3] Magnesium can be found in many foods such as grains, nuts and green leafy vegetables and it plays a key role in many fundamental biological processes as well as glucose metabolism.[4]At the molecular level, it has been suggested that hypomagnesaemia may induce altered cellular glucose transport, defective tyrosine kinase activity, insulin receptor autophosphorylation, post receptor impairment in insulin function by intracellular signalling cascade and processing, reduced pancreatic insulin secretion and worsening of insulin resistance in diabetes.[5,6-8]

In patients with T2DM, prevalence of hypomagnesemia ranges from 14 to 48% compared to 2.5-5% in healthy population.[5] This study aimed to evaluate the frequency of hypomagnesemia in hospitalized patients with T2DM and impaired glucose tolerance (IGT) and correlate with glycemic status and associated diabetic complications.

METHODS

This cross-sectional study was done at the medicine in-patient department of Bangladesh Institute of Research and Rehabilitation in Diabetes, Endocrine and Metabolic Disorders (BIRDEM) General Hospital, Dhaka, Bangladesh from November, 2016 to March, 2017. One hundred hospitalized adult patients with T2DM and IGT were included in the study. Patients, who had acute diarrhea or vomiting in previous 7 days, patients who had chronic diarrhea or malabsorpsion syndrome or who had recent history of taking diuretics were excluded from the study. Serum magnesium level <0.7 mmol/L was labeled as hypomagnesemia.[2] The study protocol was approved by the Institutional Review Board (IRB) of BIRDEM General Hospital, Dhaka, Bangladesh. Data were collected from patients and hospital records after taking informed written consents and were recorded in case record forms. Data were analyzed by Statistical Package for Social Sciences (SPSS) version 20.Qualitative data were expressed in percentage and quantitative data were expressed in mean, median, standard deviation and interquartile range. P value of <0.05 was taken as significant.

RESULTS

Total patients were 100 including 92 T2DM and 8 IGT. Mean age was 61.13 ±11.40 years with 68% being males. Base-line characteristics are shown in Table I.

Table I Baseline characteristics of the patients (N=100)

Variable	Results
Age (mean± SD) (in years)	61.13±11.4
Gender (%)	68% male, 32% female
Co-morbidities	
Hypertension (%)	86
Ischaemic heart disease (%)	27
Microvascular complications	
Retinopathy (%)	33
Nephropathy(%)	37
Neuropathy (%)	29

Among the study population, 44% patients had hypomagnesemia. Mean serum magnesium level was 0.73±0.16 mmol/L. Among patients with T2DM the frequency of hypomagnesemia was (39/92), 42.4% and among patients with IGT frequency was (5/8) 62.5%. The median (IQR) serum magnesium level in patients with T2DM was 0.77 (0.6-0.8) mmol/L and IGT was 0.6 (0.52-0.77) mmol/L (Figure 1).

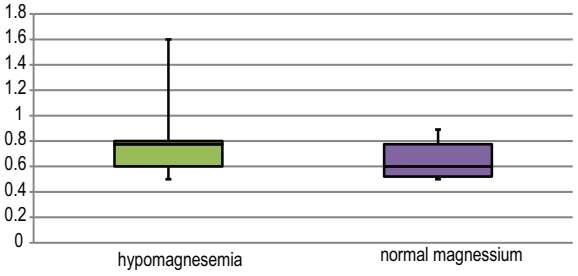

Figure 1 Level of serum magnesium (median and IQR) among patients with hypomagnesaemia and normal magnesium levels

Median HbA1c (%) (IQR) was 9.4 (7.8-12.7) in patients with hypomagnesaemia *vs* 8.85 (7.2-9.95) in patients with normal magnesium level (Figure 2). The difference was not statistically significant (p>0.05).

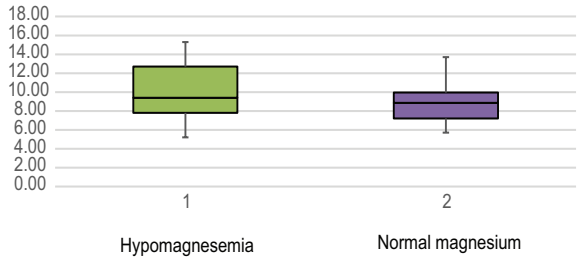

Figure 2 HbA1c among patients with hypomagnesaemia and normal magnesium level

Mean fasting blood glucose (FBG) level in study population was 9.71mmol/l and it was 9.82 mmol/l in patients with hypomagnesemia and 9.63 mmol/l in patients with normal serum magnesium level. Mean serum magnesium level in patients with FBG ≤6.0 mmol/l was 0.74 ±0.18 mmol/l and in patients with FBG >6 mmol/l mean serum magnesium was 0.73 ±0.16 mmol/l. But the difference was not statistically significant (p value >0.05). Median 2 hours post prandial blood glucose level was 12 (10.4-16.15) mmol/L in hypomagnesemia group and 11.7 (10.3-14.7) mmol/L in normal magnesium group (Figure 3), though the difference was not statistically significant.

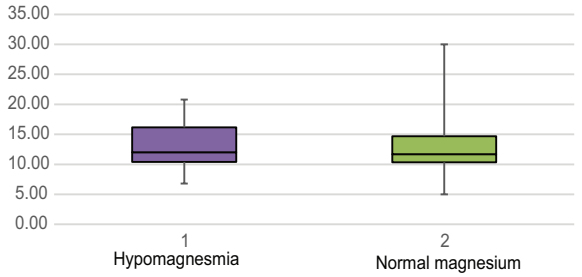

Figure 3 Post-prandial blood glucose levels among patients with hypomagnesaemia and normal magnesium level

There was negative correlation between serum magnesium and HbA1c (r-0.075), FBG (r-0.003) and post prandial blood glucose level (r-0.006) according to Pearson's formula but p value was not statistically significant (>0.05). Among the patients with hypomagnesaemia, the percentage of ischemic heart disease (IHD), diabetic retinopathy, diabetic nephropathy and diabetic neuropathy was 31.8%, 36.4%, 43.2% and 34.1% compared to 23.2%, 30.4%, 32.1% and 25% respectively in patients with normal magnesium level (Figure 4).

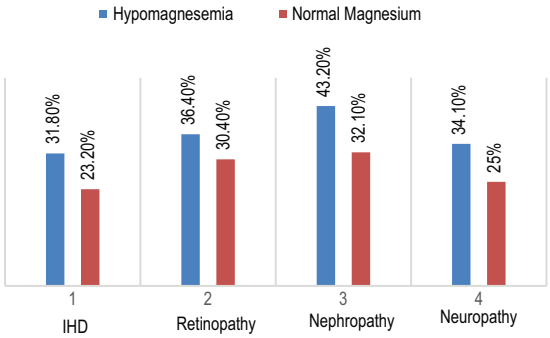

Figure 4 Different complications of diabetes among patients with hypomagnesaemia and normal magnesium level

DISCUSSION

Multiple studies have shown inverse relationship between dietary magnesium intake and risk of T2DM.[9] Several studies have shown beneficial effects of magnesium supplementation on insulin sensitivity and glucose metabolism.[10-12] A randomized double-blind placebo controlled trial in healthy individuals with prediabetes and hypomagnesemia showed that magnesium supplementation for 3 months reduced hs-CRP levels[13], given that inflammation and oxidative stress are important factors in insulin resistance, hypomagnesemia may contribute to insulin resistance.[14,15]

Rosangela Spiga et al. did a large prospective cohort study in 2019 where there were 589 participants with a mean follow up time of 5.6 years. It revealed that there was significant negative correlation between magnesium level with FBG and 2 hour post prandial plasma glucose level.[16] In our study the negative correlation was not statistically significant, but it may be attributed to small sample size. Hatice Ozcaliskan Ilkay et al. reported in a study higher level of HbA1c, fasting and post prandial plasma glucose in type 2 diabetic patients with hypomagnesemia compared to type 2 diabetic patients with normal magnesium.[17] We found similar results in our study.

Arundhati Dasgupta et al. found that hypomagnesemia was associated with poor glycemic control, retinopathy, nephropathy and foot ulcers.[18] In our study we found higher HbA1c, fasting and post prandial blood glucose as well as higher rate of IHD, retinopathy, nephropathy and neuropathy in patients with hypomagnesemia compared to normal magnesium. One study by Barbagallo M et al found that oral magnesium supplementation appears to be useful in T2DM patients with hypomagnesemia to improve insulin resistance, oxidative stress and systemic inflammation.[19]

Magnesium is found to be associated with more rapid and permanent decline of renal function.[20] Multiple epidemiological studies have shown inverse relationship between magnesium and risk of developing type 2 diabetes.[9] A randomized double blind control study showed magnesium supplementation improved insulin sensitivity and metabolic control.[21] The prevalence of hypomagnesemia is 14-48% in patients with T2DM, which means millions of people are affected worldwide.[22] Hypomagnesemia is associated with conditions that are often present in T2DM, including hypertension, hypokalemia and muscle cramps, more clinical attention is necessary to address this problem.[23] Patients with T2DM who are taking diuretics, proton pump inhibitors, calcineurin inhibitors and who suffer from diarrhoea due to diabetic neuropathy are specially at risk of hypomagnesemia and should be closely monitored.[24,25] Although widespread clinical evidence of the association of hypomagnesemia and T2DM are available[26], the molecular mechanisms of Mg2+ on insulin secretion and insulin resistance are still not properly understood.

The results of this study indicate that hypomagnesemia may be associated with poor glycemic control as well as increased rate of complications. Limitations of this study are small sample size and it was done in hospitalized patients who may have other risk factors for poor diabetes control. However, the findings are still far from complete and further studies are needed to understand the complicated role of magnesium in diabetes and the role of this nutrient as protective factor against insulin resistance and diabetic complications.

Authors' contribution: TM and MAR planned the study, TM collected and analyzed data, TM did literature search, TM and MAR drafted manuscript with contribution of WMM, MAQ and LF. All authors read and approved the final manuscript for submission.

Conflict of interest: Nothing to declare.

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