Annals of International Medical and Dental Research
E-ISSN: 2395-2822 | P-ISSN: 2395-2814
Vol-8, Issue-5 | September-October 2022
DOI: 10.53339/aimdr.2022.8.5.20
Page no- 149-158 | Section- Research Article (Medicine)

Prevalence of Hypomagnesaemia Among Type 2 Diabetic Patients Admitted to a Tertiary Care Hospital

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Received: 03 May 2022
Revised: 27 June 2022
Accepted: 04 July 2022
Published: 22 August 2022

Abstract

Background: Magnesium (Mg) is one of the dominant intracellular cations. It catalyzes more than 300 intracellular reactions and has multiple functions in areas of energy production, intracellular calcium regulation, protein synthesis and degradation, and neurotransmitter release. To estimate the prevalence of hypomagnesaemia among patients with type 2 diabetes attending a tertiary care Hospital. **Material & Methods:** A cross-sectional study was carried out at the Bangladesh Institute of Research and Rehabilitation in Diabetes (BIRDEM), which treats patients with Diabetes Mellitus from all over the country. A total of 754 patients were included and analyzed in this study. All patients with type 2 diabetes who were referred to the BIRDEM during the period from the first of July 2020 to the end of June 2021 and had their serum Mg assessed were included in the study. **Results:** Out of 754 patients with type 2 diabetes, 150 patients (19.89%) (95% CI, 16.8%-21.4%) were hypomagnesaemic. Female gender, hypertension, statin therapy, HbA1c between 7-7.9% or ≥ 9% and patients with diabetes duration more than five years were independent risk factors for hypomagnesaemia. No association between hypomagnesaemia and age distribution, smoking history, neuropathy and retinopathy was found. In comparison with individuals enrolled in the National Vitamin D study, diabetic patients in this study had a much higher prevalence of hypomagnesaemia (19% vs. 0.7%) with odd's ratio of 32 (95% CI, 21-48.2). **Conclusions:** The present study has shown that an apparently-healthy elderly population may have a magnesium deficiency that may need to be identified and treated for optimizing clinical care. Further multicentric studies with a greater sample size should be done in this field, which will benefit the elderly population.

Keywords:- Prevalence, hypomagnesemia, serum magnesium.

INTRODUCTION

Diabetes Mellitus is a group of metabolic diseases characterized by hyperglycaemia resulting from defects in insulin secretion, insulin action, or both. There are two major clinical entities; Type 1 and Type 2. Type 2 Diabetes Mellitus accounts for approximately 90% of all diabetes cases worldwide and is a global public health concern since it is on the rise due to changes in lifestyle and dietary habits.[1] International Diabetes Federation

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predicts a rise in the number of diabetes cases from 382 million (in 2013) to 592 million (in 2035). This translates to a 170% rise in developing countries against a 42% rise in developed countries, causing a great economic burden on the developing countries. The International Diabetes Federation report also revealed that 80% of diabetic people live in low- and middle-income countries and most are between 40-59years of age.[2] Motala et al in 2008 obtained a prevalence of 3.2% diabetes cases in South Africa while Christensen et al in 2009 recorded a prevalence of 4.2% diabetes cases in Kenya.[3,4] Currently, 1.2 million Kenyans live with diabetes and this number is expected to rise to 1.5 million (4.5% of the population) by 2025 as predicted by the World Health Organisation in 2009. Diabetes is the fourth commonest Non-Communicable Disease and is a major cause of morbidity and mortality the world over. The hallmark of Type 2 Diabetes is chronic hyperglycemia which is associated with long-term damage, dysfunction and failure of different organs – kidneys, heart, blood vessels, nerves, and eyes.[5] Diabetes is associated with various electrolyte imbalances including magnesium. Magnesium is the most under-diagnosed electrolyte deficiency and has been referred to as 'the essential forgotten electrolyte.[6] Type 2 Diabetes Mellitus is a recognized independent risk factor for hypomagnesaemia with a reported incidence of 13.5-47.7%.[7] It is associated with both extracellular and intracellular magnesium deficits; the principal causes of magnesium loss are gastrointestinal and renal losses.[8] Notably, the kidney is the principal site for magnesium homeostasis. Hypomagnesaemia has been implicated in Type 2 Diabetes morbidity and its complications; there is an established association between hypomagnesaemia, poor glycaemic control and diabetes-related complications including deterioration in renal function.[9] Oral magnesium supplementation is beneficial since it restores magnesium levels and improves insulin sensitivity and glycaemic metabolic control eventually slowing down the rapid progression into diabetes-related complications.[10] It is, therefore, necessary to regularly monitor serum magnesium levels ideally in all Type 2 Diabetes patients but more so amongst those with poor metabolic control and those with diabetes-related complications. Hypomagnesemia in critically ill diabetic patients is associated with high mortality.[11] The prevalence of hypomagnesaemia in our diabetic population remains largely unknown yet most of our diabetic patients have poor metabolic control. A cross-sectional study carried out by Omari et al in 2013 to assess the level of knowledge, self-care practice and glycaemic control among Type 2 diabetes patients attending the diabetes outpatient clinic in KNH, revealed that only 29.5% of the patients achieved glycosylated haemoglobin equal to or less than 7%. With the documented prognostic implications of magnesium deficiency and the beneficial effects of magnesium supplementation, it is therefore prudent to know the magnitude of hypomagnesaemia in our Type 2 Diabetes patients. The aim of study was to estimate the prevalence of hypomagnesaemia among patients with type 2 diabetes attending a tertiary care Hospital.

MATERIAL AND METHODS

A cross-sectional study was carried out at the Bangladesh Institute of Research and Rehabilitation in Diabetes (BIRDEM), which treats patients with Diabetes Mellitus from all

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over the country. A total of 754 patients were included and analyzed in this study. All patients with type 2 diabetes who were referred to the BIRDEM during the period from the first of July 2020 to the end of June 2021 and had their serum Mg assessed were included in the study. Patients with the following conditions were excluded from the study: pregnancy, hyperthyroidism, hypoparathyroidism, celiac disease, renal failure, chronic use of steroid medication, antacids and purgatives. Data were obtained from the medical records, which were abstracted by the investigator using a data sheet prepared for this study. Waist to height ratio was considered normal if waist to height ratio was ≤0.5, and elevated if it was > 0.5. BMI was expressed as the quotient between weight (kg) and height squared (m2). Patients were classified according to BMI following the recommendation of the World Health Organization as adopted by the American Diabetes Association (12). Readings of systolic and diastolic blood pressures were taken while the subjects were seated and the arm was kept at the heart level, after at least five minutes of rest, using a standardized mercury sphygmomanometer, high blood pressure was defined as systolic blood pressure ≥130 mmHg or diastolic blood pressure ≥80 mmHg or if the patient was already on antihypertensive drugs (13). Metabolic abnormalities were defined according to the American Diabetes Association 2011 (13) as follows: total serum cholesterol ≥200 mg/dL, serum LDL ≥100mg/dL, serum triglyceride ≥150 mg/dL, serum HDL ≤40 mg/dL in men, and ≤50 mg/dL in women, or if the patient was already on anti-dyslipidemic agents. Smoking was classified into three categories according to WHO guidelines 1998; current smoker was defined as: a person who smokes cigarettes daily or occasionally; past-smoker: a person who formerly was a daily or occasional smoker, but currently does not smoke at all; non-smoker: a person who has never smoked before or has smoked very little in the past.[14] Diabetes mellitus was diagnosed if the patient had an FPG ≥126 mg/dL (7.0 mmol/L) on two occasions or if the patient had a random plasma glucose ≥200 mg/dL (11.1 mmol/L) in the presence of classical symptoms of hyperglycemia, or if he or she had HbA1c ≥ 6.5%. Moreover, diabetes was considered to be controlled if the patient had HbA1c <7.0% according to the American Diabetes Association (ADA) 2011 guidelines.[13] Magnesium was measured by the "Colorimetric Endpoint Method" using Roche/Cobas Integra 800 automated system. The imprecision, with run (CV), was 2.8 and 2.9% between runs as judged by internal quality-control systems. Our operational definition of hypomagnesae was the occurrence of magnesium levels below 1.7 mg/dL (normal range 1.7-2.55 mg/dL). This normal range of magnesium (1.7-2.55 mg/dL) is the normal value provided by our laboratory as there is no published data regarding the normal magnesium values for Jordanian yet. Retinopathy was diagnosed if it was documented by either the ophthalmologist or the treating physician in the medical records, or if the patient had received laser treatment whereas neuropathy was diagnosed if there were any of the following symptoms (numbness, tingling, or pain in toes, feet, legs, hands, arms, and fingers) in the patient's medical records or if the patient had done Nerve Conduction Study (NCS) which proves the presence of diabetic neuropathy or if the patient was receiving treatment for the above condition. Patients who had insufficient data in

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their files regarding the presence of neuropathy and retinopathy received phone calls asking them if they have had symptoms of neuropathy or retinopathy or if they had laser treatment in the case of retinopathy. Statistical Analysis Data were entered and analyzed using the Statistical Package for Social Science (SPSS). The overall prevalence of hypomagnesaemia was calculated also in the subgroups defined by relevant variables. The bivariate association between hypomagnesaemia and several variables was assessed for statistical significance using the chi-square test. Multivariate logistic regression was used to assess the independent effect of a given variable after adjusting for potential confounders. A P-value of < 0.05 was considered statistically significant.

RESULTS

It is a cross-sectional study, a total of 754 patients were included and analyzed in this study. [Table 1] shows the sociodemographic and anthropometric characteristics of the study population; more than 40% of patients were from the age range of 60-75 years, 467(63.13%) patients were females and 278(36.87%) were males. Most of the patients were employed about 84.62%. Almost 50% of patients had diabetics <5 years, 30.64% had diabetes for more than 10 years and 22.02% of patients had diabetics 5-10 years. A positive sign is that almost 70% of patients were non-smokers [Table 1]. [Table 2] shows the clinical characteristics of the study population; 548(72.68%) patients had hypertension and 206(27.32%) had no hypertension, 521(69.10%) patients had dyslipidemia and 233(30.90%) patients had no dyslipidemia. The mean±SD of HbA1c is 7.9±2.7. More than 90% of patients were on loop diuretics, 568(75.33%) patients were on thiazide diuretics and 432(57.29%) patients were on a statin [Table 2]. The bar diagram [Figure 1] shows the prevalence of hypomagnesaemia among type 2 diabetics; 604(80.11%) patients had hypomagnesaemia and 150(19.89%) patients hadn't. Table 3 describes the prevalence of Hypomagnesaemia in Patients with Type 2 Diabetics according to the Relevant Demographic and Clinical Characteristics.

Table 1: Sociodemographic and Anthropometric Characteristics of the Study Participants (N=754.)

Category	Frequency	Proportion
Age Distribution (Years)		
<45	95	12.60
45-60	266	35.28
60-75	321	42.57
>75	72	9.55
Gender Distribution		
Male	278	36.87
Female	476	63.13
Employment status		
Employed	638	84.62
Unemployed	116	15.38

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Duration of Diabetes (Years)		
<5	357	47.35
(5-10)	166	22.02
>10	231	30.64
Smoking		
Non-Smoker	508	67.37
Past Smoker	85	11.27
Current Smoker	161	21.35

Table 2: Clinical Characteristics of the Study Participants (N =754).

Category	**Frequency**	**Proportion**
Hypertension		
Yes	548	72.68
No	206	27.32
Dyslipidemia		
Yes	521	69.10
No	233	30.90
Neuropathy		
Yes	307	40.72
No	447	59.28
Retinopathy		
Yes	256	33.95
No	498	66.05
HbA1c, %, mean±SD = 7.9±2.7		
<7	271	35.94
7-7.9	196	25.99
8-8.9	131	17.37
>9	156	20.69
Patients on loop diuretics		
Yes	65	8.62
No	689	91.38
Patients on thiazide diuretics		
Yes	186	24.67
No	568	75.33
Patients on statin		
Yes	432	57.29
No	322	42.71

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Page no- 149-158 | Section- Research Article (Medicine)

Table 3: Prevalence of Hypomagnesaemia in Patients with Type 2 Diabetics according to the Relevant Demographic and Clinical Characteristics (N = 754)

Category	Frequency	Proportion	P-value
Age			
<45	33	4.38	0.109
45-60	42	5.57	
60-75	64	8.49	
>75	11	1.46	
Gender			
Male	49	6.5	0.0001
Female	101	13.4	
Smoking			
Non Smoker	77	10.21	0.002
Past Smoker	27	3.58	
Current Smoker	46	6.1	
Duration of Diabetes (Years)			
<5	83	11.01	0.0001
(5-10)	39	5.17	
>10	28	3.71	
Dyslipidemia			
Yes	116	15.38	0.022
No	34	4.51	
Hypertension			
Yes	111	14.72	0.00002
No	39	5.17	
Retinopathy			
Yes	54	7.16	0.002
No	96	12.73	
HbA1c, %, mean ± SD= 7.9 ± 2.7			
<7	41	5.44	0.0001
7-7.9	55	7.29	
8-8.9	27	3.58	
>9	27	3.58	
Neuropathy			
Yes	76	10.08	0.0263
No	86	11.41	
Patients on loop diuretics			
Yes	12	1.59	0.01
No	138	18.3	
Patients on thiazide diuretics			
Yes	57	7.56	0.007

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Page no- 149-158 | Section- Research Article (Medicine)

No	93	12.33	
Patients on statin			
Yes	123	16.31	0.0009
No	27	3.58	

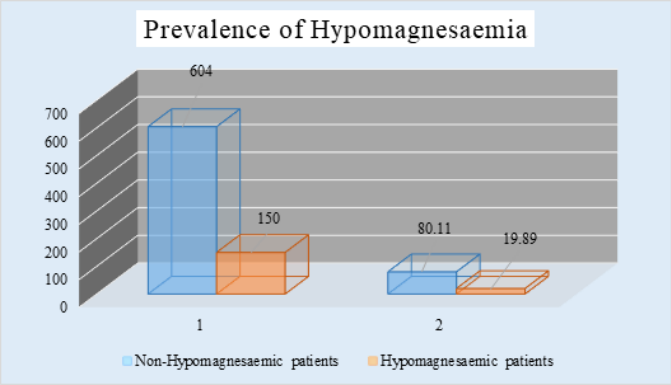

Figure 1: Prevalence of Hypomagnesaemia among Type 2 Diabetic.

DISCUSSION

In the present study low serum magnesium level among type 2 diabetic patients attending the (NCDEG) was found to be 19% (95% CI, 16.8%-21.4%) which was much higher than that observed among non-diabetics in the population-based National Vitamin D study (0.7%) (95% CI, 0.48%-1.07%). In another population-based study conducted in Iran, the prevalence of hypomagnesaemia was much higher than the results found in the Jordanian National Vitamin D Study (4.6% vs. 0.7%), respectively.[15] A higher prevalence rate of hypomagnesaemia in diabetic patients was also reported by other studies. For instance, a cross-sectional study conducted by Seyoum et al.[16] included a total of 159 subjects (44 patients with type 1 DM, 69 patients with type 2 DM and 46 non-diabetic control) to assess the prevalence of hypomagnesaemia in Ethiopian patients with type-1 and type-2 DM. The study revealed that hypomagnesaemia was present in 65% of patients with diabetes. In other studies, hypomagnesaemia has been shown to occur in 25-38% of patients with diabetes, especially in those without good metabolic control.[16,17,18,19,20] This wide range of differences in the prevalence between our study and other studies might be due to differences in the definition of hypomagnesaemia, techniques of magnesium measurements, and heterogeneity of the selected patient populations. The mechanisms responsible for hypomagnesaemia in diabetic patients are not fully understood. Osmotic diuresis accounts for a portion of magnesium loss; however, magnesium intake may also play a role in magnesium deficiency. Suppressed levels of intracellular magnesium have been reported in patients with diabetes, and it has been suggested that circulating blood glucose independent of insulin levels, is a physiologic determinant of cellular ion hemostasis, suppressing intracellular free magnesium. Additionally, in patients with insulin resistance, hyperinsulinemia itself might contribute to magnesium depletion.[21] Hypomagnesaemia was more prevalent in females in our study (25%) compared to males (12%). On further analysis, we found factors that could affect the prevalence of hypomagnesaemia are different among men and women, and we have no explanation for these gender differences, thus further studies are certainly indicated. Other studies conducted by Ascaso J F et al.[22] and Sheehan J P et al.[23] have also reported a higher

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Page no- 149-158 | Section- Research Article (Medicine)

prevalence of hypomagnesaemia in women compared to men at a 2:1 ratio. Our study had shown that the rate of hypomagnesaemia was generally increased with increasing HbA1c from only 13% of patients with HbA1c < 7%, to 25% of those with HbA1c between 7-7.9%, 19% of those with HbA1c between 8-8.9% and 22% of those with HbA1c ≥ 9% (P-value = 0.001). This study also showed that hypomagnesaemia was significantly associated with increasing duration of diabetes: patients who had diabetes between 5-9 years or ≥ 10 years had a prevalence rate of hypomagnesaemia of 24% and 23%, respectively, compared to only 12% of those in whom diabetes duration was < 5 years. Our findings are consistent with the findings of Shaikh et al.[24] who evaluated the frequency of hypomagnesaemia in patients with type 1 and type2 DM. A Total of 100 diabetic patients were studied (77 with type 2DM and 23 with type 1DM). Hypomagnesaemia was identified in 8 (14.5%) of patients with type 1 diabetes and 47 (85.5%) of patients with type 2 diabetes. Of 55 hypomagnesaemic diabetic patients, the Hemoglobin A1c (HbA1c) was raised in 40 (72.7%) patients. Shaikh et al.[25] also found that hypomagnesaemia was most prevalent in those who had diabetes duration between 6-10 years and 11-15 years (prevalence rate was 71% and 72%, respectively) compared to only 36% of patients with diabetes duration between 3 to 5 years. A close relationship between metabolic control and hypomagnesaemia was confirmed by Fujii et al.[25] who found that hypomagnesaemia was particularly present in diabetic patients with advanced retinopathy and uncontrolled diabetes. However, no significant association was noticed between hypomagnesaemia and diabetes complications in our study. Our findings are also in contrast to the finding of Devalk et al.[26] who supported the association between hypomagnesaemia and progression of retinopathy in diabetic patients using insulin. Additionally, McNair et al.[27] also reported that retinopathy occurs more in magnesium deficient patients with insulin-dependent diabetes mellitus (IDDM) and suggested hypomagnesaemia as a potential risk factor in the development and deterioration of diabetic retinopathy. An important finding of this study is the significant association between hypomagnesaemia and hypertension which was independent of the potential confounding factors. Our data seem to support Resnick's hypothesis suggesting that hypomagnesaemia in diabetic patients,[28] which seems to be accentuated by the presence of hypertension, could explain the missing link between diabetes and hypertension. An association between hypomagnesaemia and the use of lipid-lowering agents was also noticed in our study. Such a finding is consistent with the findings of Haenni et al.[29] who reported that mean total serum magnesium concentration decreased following the treatment with Gimfibrazole and Simvastatin in patients with noninsulin-dependent diabetes mellitus (NIDDM).

Limitations of the study

The study was conducted in a single hospital with a small sample size. So, the results may not represent the whole community.

CONCLUSIONS

Although the prevalence recorded appears to be low compared to studies done in other regions, there is still a significant burden of hypomagnesemia among our diabetic patients. Patients with hypomagnesemia were noted to

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Page no- 149-158 | Section- Research Article (Medicine)

have poorer glycaemic control and a longer mean duration of diabetes. Larger and longitudinal studies to determine the direction of association between hypomagnesemia and: glycaemic control and renal function reserve.

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Annals of International Medical and Dental Research
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Page no- 149-158 | Section- Research Article (Medicine)

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Source of Support: Nil, Conflict of Interest: None declared