ORIGINAL ARTICLE

ASSOCIATION BETWEEN LOW SERUM MAGNESIUM LEVEL AND TYPE 2 DIABETES MELLITUS IN ABBOTTABAD

Mohammad Munir Noor, Quratulann Nazir*, Tariq Mehmood Khan, Saima Gillani***, Munir Ahmad Abbasi†, Abdur Rauf††, Zaheer Uddin Qureshi†††**

Department of Medicine, Women Medical College, Abbottabad, *Department of Gynaecology, Ayub Teaching Hospital, Abbottabad, **Department of Pharmacology & Therapeutics, Frontier Medical College, Abbottabad, ***Department of Paediatrics, ††Department of Medicine, ††Department of Surgery, Ayub Teaching Hospital, Abbottabad, †Department of Pulmonology, Fauji Foundation Hospital, Rawalpindi-Pakistan

Background: Magnesium serves as a cofactor for various oxidation reactions in the body and helps in glucose transport across cell membrane. Deficiency of magnesium is a common electrolyte abnormality in type 2 diabetic patients and is linked to development of various diabetic complications. This study was conducted to determine the association between low serum magnesium level and type 2 diabetes mellitus presenting at Medical B ward, BBS Hospital Abbottabad. **Methods**: This descriptive study was conducted over a period of 6 months starting July 1, 2017. One hundred & eighty diagnosed diabetic patients aged at least 40 years, were included in the study. Their serum magnesium level was checked after withdrawing blood under strict aseptic conditions. Fasting & random blood glucose and the level of glycosylated haemoglobin were measured and age, gender, duration of illness were recorded on a proforma. **Results**: Sixty-one patients (33.89%) had hypomagnesemia. There was no significant association between hypomagnesemia and age and sex of patients (p>0.05). However, hypomagnesemia was found to be significantly associated with the duration of diabetes mellitus among study population (p=0.02). **Conclusion**: Hypomagnesemia is frequently present in patients with diabetes mellitus and it appears that its prevalence increases with the duration of diabetes mellitus.

Keywords: Type 2 Diabetes Mellitus; Serum Magnesium levels; electrolyte disturbance; HbA1C

Citation: Noor MM, Nazir Q, Khan TM, Gillani S, Abbasi MA, Rauf A, *et al*. Association between low serum magnesium level and type 2 diabetes mellitus in Abbottabad. J Ayub Med Coll Abbottabad 2019;31(2):226–9.

INTRODUCTION

The human body acquires its daily required dose of minerals from ingested food and drinks and Magnesium is the fourth most common cation found in the body and second most common intracellular cation in vertebrate bodies.[1] Magnesium plays an important role in a number of oxidative processes in the body in addition to facilitating transport of glucose across the cell membrane as a cofactor.[2] Normal serum magnesium levels stay in the range of 0.75–0.95 mmol/l (1.7–2.3 mg/dl).[2] Hypomagnesemia is a frequent finding in hospitalized patients and is found in as much as 12% of hospitalized patients.[3] Compared to general non-hospitalized population where prevalence of hypomagnesemia ranges from 2.5–15% it is much more common (13.5–47.7%) in diabetic patients, particularly those with type 2 diabetes mellitus hospitalized for one reason or another.[4] Interestingly, presence of hypomagnesemia has been found to confer an increased risk of diabetes mellitus.[5] However, endocrine and metabolic disorders such as hypothyroidism, Cushing's syndrome and insulin resistance have also been found to be associated with deficiency of magnesium in the body.[6,7]

Currently the mechanisms by which a deficiency of magnesium induces or worsens hyperglycaemia / diabetes are not known however, it is thought that reduction in intra-cellular magnesium level leads to impairment of tyrosine kinases, glucose transport across cell membranes, post-receptor effects of insulin as well as reduction in secretion of insulin from pancreatic B cells.[8] Hypomagnesemia has also been implicated in the pathogenesis of dyslipidaemias, atherosclerosis, hypertension and coronary artery disease in addition to increase in oxidative stress and inflammation, impairment of clotting cascade and thickness of carotid artery walls.[8] Additionally, development of a number of macrovascular complications of diabetes mellitus has been attributed to hypomagnesemia. Infect, a diagnosis of hypomagnesemia increases an all-cause mortality risk in type-2 diabetic patients.[9]

The reported prevalence of hypermagnesemia in diabetic patients is in the range of 47.7–65%.[8] Loss of magnesium due to osmotic diuresis is frequently responsible for hypomagnesemia seen in diabetic patients.[10] Role of glycosuria by causing impaired re-absorption of magnesium in in the renal tubules has also been described.[11] In addition to its association with type-2 diabetes mellitus, hypomagnesemia is related inversely with the glycaemic control.[12,13] Some authors have suggested that a high dietary intake of Magnesium leads to a lower risk of type-2 diabetes

mellitus.[13] Diabetic patients with hypomagnesemia have been observed to have poor control of their blood glucose levels, increased resistance to insulin and they tend to show a relatively earlier development of various macrovascular and microvascular complications of diabetes mellitus.[12–15]

In the light of aforementioned facts, we decided to conduct a study on to determine the frequency of hypomagnesemia in our local diabetic population since there is no local data regarding magnesium deficiency in diabetic patients from our region.

MATERIAL AND METHODS

This descriptive cross-sectional study was conducted over a period of six months with an aim to determine an association between hypomagnesemia and type 2 diabetes mellitus in adult type 2 diabetic patients presenting to our hospital. Normal serum magnesium levels stay in the range of 0.75–0.95 mmol/l (1.7–2.3 mg/dl).[2] and for the purpose of study, hypomagnesemia was defined as measurement of serum magnesium levels less than 0.6 mmoL/L (1.7mg/dl), determined by calmagite dye method using autoanalyzer. For this study, a sample size of 180 patients was calculated keeping confidence level of 95%, taking the prevalence of hypomagnesemia in type 2 diabetics to be 13.5%.[4], and absolute precision of 5%. The study cohort was enrolled by consecutive (non-probability) sampling. All diabetic men and women aged 40 years to 70 years who presented for consultation in the OPD of Benazir Bhutto Shaheed (DHQ) Hospital were enrolled in the study after obtaining an informed consent.

Patients with a clinical evidence of malabsorption, currently on enteral or parenteral nutritional support, with a history of diuretic use or use of magnesium containing antacids in past 2 weeks, with active pulmonary tuberculosis, acute coronary syndrome or decompensated cardiovascular disease, end-stage renal disease with a GFR <50 ml/min and patients with cirrhosis of liver were excluded from this study. After obtaining a thorough medical history and a physical examination, blood was drawn from the antecubital vein of the patients under strict aseptic conditions for measurement of serum magnesium, random blood glucose as well as the glycosylated haemoglobin. The collected data were entered into and analyzed using SPSS version 20.0. Mean±SD were calculated for numerical variables while frequencies and percentages were calculated for numerical variables. The outcome variable, i.e., hypomagnesemia was stratified according to age, gender of patients and the duration of diabetes mellitus to see effect modification. Independent samples t-test was used at 5% significance level to see differences in Mg level in both genders.

RESULTS

This cross-sectional study was conducted at BBS Hospital, Abbottabad from July to December 2017. The study population comprised of 180 adults, both males and females, aged 40–70 years. There were 94 (52.22%) males and 86 (47.78%) females in the study population. The mean age of study participants was 57.68±6.61 years with a range of 46–68 years. The mean duration of diabetes mellitus was 12.34±2.77 years with a range of 8–17 years. The mean fasting and random blood glucose level of study participants was 112.31±10.34 and 209.54±26.33 mg/dl respectively. Likewise, the mean serum magnesium level was 1.80±0.27 mg/dl and the mean glycosylated haemoglobin level was 7.46±0.42 among study participants. Overall 61 (33.89%) patients were found to have hypomagnesemia.

When hypomagnesemia was stratified according to age, sex and duration of diabetes mellitus, a significant association was found between duration of diabetes mellitus and hypomagnesemia (p<0.05).

There was no significant difference in the serum magnesium levels among males (Mg=1.66, SD=0.48) and females (Mg=1.7, SD=0.5); t (178) =-0.05, p=0.96 (p>0.05).

Table-1: Serum Magnesium Levels in study participants

Number	180
Mean	1.80
Standard Deviation	0.27
Minimum	1.40
Maximum	2.20

Table-2: Cross-tabulation of hypomagnesemia and age of study participants

Hypomagnesemia	**Age of study participants**		**Total**	***p*-value**
	Upto 55 years	> 55 years		
Yes	26.00	35.00	61.00	0.77
No	48.00	71.00	119.00	
Total	74.00	106.00	180.00	

p-value < 0.05

Table-3: Cross tabulation of hypomagnesemia and sex of study participants

Hypomagnesemia	**Sex of patients**		**Total**	***p*-value**
	Male	Female		
Yes	32.00	29.00	61.00	0.96
No	62.00	57.00	119.00	
Total	94.00	86.00	180.00	

p-value <0.05

Table-4: Cross-tabulation of Hypomagnesemia and duration of diabetes Mellitus among study participants

Hypomagnesemia	**Duration of diabetes mellitus**		**Total**	***p*-value**
	upto 10 years	> 10 years		
Yes	25.00	36.00	61.00	
No	28.00	91.00	119.00	0.02*
Total	53.00	127.00	180.00	

p-is significant at <0.05

DISCUSSION

The poor metabolic control in diabetics, particularly in type 2 diabetes mellitus, is known to affect the serum magnesium concentration predisposing these patients to development of hypomagnesemia. The development of hypomagnesemia is, in turn, reported to be responsible for some of the micro- and / or macroangiopathies characteristic of diabetes mellitus.[13,16,17]

In our study the serum magnesium level of sixty-one patients (33.89%) was found to be below the cut-off point indicating hypomagnesemia in those patients. The reported prevalence of hypomagnesemia in the literature is in range of 25–39% while a study from Pakistan reported that hypomagnesemia was found in 117 (36.22%) of their study cohort.[8] Another study from Hyderabad, Pakistan reported that hypomagnesemia was detected in 55% of study population while another study from Karachi, Pakistan reported that the frequency of hypomagnesemia in type 2 diabetic patients was 30%.[18,19] A Swiss study which studied serum magnesium level in 109 diabetic patients with type 2 diabetes mellitus and 156 healthy controls reported that 41 (37.6%) patients with type 2 diabetes mellitus had hypomagnesemia.[20]

As has been noted earlier, magnesium deficiency is commonly found in about 7–11% of hospitalized patients[21,22], and it is more common in diabetic patients, it is not surprising that as much as 65% of critically ill patients have magnesium deficiency.[23–25] The exact mechanisms underlying deficiency of magnesium in diabetes mellitus are unclear as of now, however a number of propositions include decreased dietary content of magnesium, poor or faulty absorption from the gut and increased loss in urine as a result of hyperglycaemia and / or osmotic diuresis.[10,26,27]

A study from Brazil showed that presence of hypomagnesemia in diabetics was associated with earlier development of micro- and macro-vascular complications of diabetes mellitus, and that glycaemic control in diabetics could be improved by extra supplementation with magnesium.[13]

Although serum magnesium deficiency has been correlated with poor glycaemic control[28], we did not determine this association and this is one of the limitations of this study. However, we did find that hypomagnesemia was significantly associated with longer duration of disease. Interestingly, the duration of diabetes was not found to be a significant predictor of hypomagnesemia.[8,18] Similar to these reports, we did not find any association between hypomagnesemia and age and sex of diabetic patients.[8,18]

CONCLUSION

There was a significant association between hypomagnesemia and type 2 diabetes mellitus in our study, therefore, magnesium levels should be performed and correlated in every patient type 2 diabetic patient. However, there were a number of study limitations which make interpretation of above results difficult. Our study sample size was small; we didn't document relationship between glycaemic control and hypomagnesemia; we didn't study the role played by hypomagnesemia in development of various micro- and macrovascular complications of diabetes mellitus. Therefore, it is recommended that further studies with a larger sample size should be conducted to determine the true spectrum of magnesium deficiency in diabetic patients of our region.

AUTHORS' CONTRIBUTION

MMN: Study design, data collection, literature review. QN: Study design, drafting. TMK & SG: Literature review. MAA: Data analysis, draft revision. AR & ZUQ: Data analysis, literature review

REFERENCES

1. Voma C, Romani AMP. Role of Magnesium in the Regulation of Hepatic Glucose Homeostasis. In: Szablewski L, editor. Glucose Homeostasis [Internet]. InTech; 2014 [cited 2018 Jan 20]. Available from: http://www.intechopen.com/books/glucose-homeostasis/role-of-magnesium-in-the-regulation-of-hepatic-glucose-homeostasis
2. Musso CG. Magnesium metabolism in health and disease. Int Urol Nephrol 2009;41(2):357–62.
3. Villegas R, Gao YT, Dai Q, Yang G, Cai H, Li H, *et al*. Dietary calcium and magnesium intakes and the risk of type 2 diabetes: the Shanghai Women's Health Study. Am J Clin Nutr 2009;89(4):1059–67.
4. Lima M de L, Cruz T, Rodrigues LE, Bomfim O, Melo J, Correia R, *et al*. Serum and intracellular magnesium deficiency in patients with metabolic syndrome--evidences for its relation to insulin resistance. Diabetes Res Clin Pract 2009;83(2):257–62.
5. Nair A, Hocher B, Pfab T, Konrad M, van Zeeland F, Bindels R, *et al*. Two Genetic Variants of TRPM6 Increase Risk for Hypomagnesemia Associated with Diabetes Mellitus Type 2. Biophysic J 2011;100(3):87a.
6. Mahalle N, Garg MK, Kulkarni MV, Naik SS. Relation of magnesium with insulin resistance and inflammatory markers in subjects with known Coronary artery disease. J Cardiovasc Dis Res 2014;5(1):22.
7. Sakaguchi Y, Shoji T, Hayashi T, Suzuki A, Shimizu M, Mitsumoto K, *et al*. Hypomagnesemia in type 2 diabetic nephropathy: a novel predictor of end-stage renal disease. Diabetes Care 2012;35(7):1591–7.
8. Siddiqui MU, Ali I, Zakariya M, Asghar SP, Ahmed MR, Ibrahim GH. Frequency of hypomagnesemia in patients with uncontrolled type ii diabetes mellitus. Pak Armed Forces Med J 2016;66(6):845–50.
9. Lecube A, Baena-Fustegueras JA, Fort JM, Pelegrí D, Hernández C, Simó R. Diabetes is the main factor accounting for hypomagnesemia in obese subjects. PLoS One 2012;7(1):e30599.

10. Lee CT, Lien YH, Lai LW, Chen JB, Lin CR, Chen HC. Increased renal calcium and magnesium transporter abundance in streptozotocin-induced diabetes mellitus. Kidney Int 2006;69(10):1786–91.
11. Groenestege WMT, Hoenderop JG, van den Heuvel L, Knoers N, Bindels RJ. The epithelial Mg2+ channel transient receptor potential melastatin 6 is regulated by dietary Mg2+ content and estrogens. J Am Soc Nephrol 2006;17(4):1035–43.
12. Pham PCT, Pham PMT, Pham SV, Miller JM, Pham PTT. Hypomagnesemia in patients with type 2 diabetes. Clin J Am Soc Nephrol 2007;2(2):366–73.
13. Pham PCT, Pham PMT, Pham PA, Pham SV, Pham HV, Miller JM, *et al*. Lower serum magnesium levels are associated with more rapid decline of renal function in patients with diabetes mellitus type 2. Clin Nephrol 2005;63(6):429–36.
14. Van Dam RM, Hu FB, Rosenberg L, Krishnan S, Palmer JR. Dietary calcium and magnesium, major food sources, and risk of type 2 diabetes in U.S. black women. Diabetes Care 2006;29(10):2238–43.
15. Bo S, Pisu E. Role of dietary magnesium in cardiovascular disease prevention, insulin sensitivity and diabetes. Curr Opin Lipidol 2008;19(1):50–6.
16. McNair P, Christiansen C, Madsbad S, Lauritzen E, Faber O, Binder C, *et al*. Hypomagnesaemia - a risk factor in diabetic retinopathy. Diabetes 1978;27(11):1075–7.
17. Sales CH, Pedrosa Lde F. Magnesium and diabetes mellitus: their relation. Clin Nutr 2006;25(4):554–62.
18. Shaikh MK, Devrajani BR, Soomro AA, Ali Shah SZ, Devrajani T, Das T. Hypomagnesemia in Patients with Diabetes mellitus. World Appl Sci J 2011;12(10):1803–6.
19. Hasan M, Sultan S, Ashfaq S, Irfan SM. Hypomagnesemia in Type II Diabetes Mellitus Patients; An Experience From a Tertiary Care Center. Ann Pak Inst Med Sci 2017:13(2);144–8.
20. Wälti MK, Zimmermann MB, Spinas GA, Hurrell RF. Low plasma magnesium in type 2 diabetes. Swiss Med Wkly 2003;133(19-20):289–92.
21. Whang R, Oei TO, Aikawa JK, Watanabe A, Vannatta J, Fryer A, *et al*. Predictors of clinical hypomagnesemia. Hypokalemia, hypophosphatemia, hyponatremia, and hypocalcemia. Arch Intern Med 1984;144(9):1794–6.
22. Hayes JP, Ryan MF, Brazil N, Riordan TO, Walsh JB, Coakley D. Serum hypomagnesaemia in an elderly day-hospital population. Ir Med J 1989;82(3):117–9.
23. Ryzen E. Magnesium homeostasis in critically ill patients. Magnesium 1989;8(3-4):201–12.
24. Noronha JL, Matuschak GM. Magnesium in critical illness: metabolism, assessment, and treatment. Intensive Care Med 2002;28(6):667–79.
25. Chernow B, Bamberger S, Stoiko M, Vadnais M, Mills S, Hoellerich V, *et al*. Hypomagnesemia in patients in postoperative intensive care. Chest 1989;95(2):391–7.
26. Wälti MK, Zimmermann MB, Spinas GA, Jacob S, Hurrell RF. Dietary magnesium intake in type 2 diabetes. Eur J Clin Nutr 2002;56(5):409–14.
27. McNair P, Christensen MS, Christiansen C, Madsbad S, Transbøl I. Renal hypomagnesaemia in human diabetes mellitus: its relation to glucose homeostasis. Eur J Clin Invest 1982;12(1):81–5.
28. Schlienger JL, Grunenberger F, Maier EA, Simon C, Chabrier G, Leroy MJ. Disorders of plasma trace elements in diabetes. Relation to blood glucose equilibrium. Presse Med 1988;17(21):1076–9.

Submitted: 24 September, 2018	*Revised: 13 January, 2019*	*Accepted: 23 January,2019*

Address for Correspondence:

Dr. Mohammad Munir Noor, Department of Medicine, Women Medical College, Abbottabad-Pakistan
Cell: +92 300 811 1090
Email: anni_5055@yahoo.com