

RESEARCH ARTICLE

Role of serum magnesium level as an indicator of glycemic control in type 2 diabetes mellitus

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ABSTRACT

Background: Diabetes mellitus (DM) is caused by various etiological factors that lead to different metabolic dysregulations. Magnesium (Mg) is supposed to have some role in glycemic control in Type 2 diabetes and also with the disease progression. This study was taken up to estimate the level of serum Mg and correlate the same with glycated hemoglobin (HbA1c). **Aim and Objective:** The present study was conducted to estimate serum Mg level in type 2 DM patients and find out if there is any correlation with HbA1c. **Materials and Methods:** Blood samples from 50 patients of type 2 diabetes were taken and levels of different parameters – fasting blood sugar, postprandial blood sugar, HbA1c, and serum Mg were estimated and analyzed statistically. **Results:** The mean serum Mg in cases is 1.64 ± 0.15 mg/dl and mean serum Mg in controls is 1.9 ± 0.16 mg/dl. Mean HbA1c in cases is $7.49 \pm 1.22\%$ and mean HbA1c in controls is $4.64 \pm 0.36\%$. There is a negative correlation between serum Mg levels and HbA1c. **Conclusion:** In this study, inverse correlation was found between serum Mg level and HbA1c. Further larger study will be needed to strengthen the results revealed.

KEY WORDS: Serum Magnesium; Glycated Hemoglobin; Fasting Blood Sugar; Diabetes Mellitus


INTRODUCTION

Diabetes mellitus (DM) is caused by various etiological factors that lead to different metabolic dysregulations. It is a combination of diverse group of metabolic disarray with events of hyperglycemia and glucose intolerance as a result of either deficient production of insulin, ineffective insulin action, or a combination of both.^[1] Depending on the etiopathogenesis and mode of clinical presentation, it can

broadly be divided into four types or classes: Type 1 DM, Type 2 DM, gestational DM, and other specific types.^[1]

Magnesium (Mg) by being a cofactor for various enzymes of metabolism,^[2] including the enzymes of glycolysis, plays a very pertinent role in the body. It is also required for regulation of insulin signaling and post-receptorial action of insulin. Low serum Mg status has been seen in many Type 2 DM patients by different observers. The reason is attributed mainly due to enhanced renal excretion and may also be due to reduced dietary intake.^[3]

Mg is also involved in insulin-mediated uptake of glucose.^[4] Certain studies have reported that deficiency of Mg may induce an altered state of cellular glucose transport, decreased pancreatic insulin secretion, and defective post-receptorial action of insulin.^[5-8]

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Therefore, Mg is important for glucose homeostasis and its deficiency can negatively impact and worsen the insulin resistance in type 2 DM. Its deficiency in diabetes has been associated with endothelial cell dysfunction, inflammation, and oxidative stress, which leads to vascular complications such as nephropathy and atherosclerosis.^[9]

A previous study by Sharma *et al.*^[10] carried out to assess the connection between serum Mg and complications of DM showed that duration of DM was negatively related and poor glycemic control was associated with hypomagnesemia.

Ankush *et al.*^[11] have found that hypomagnesemia was more pronounced in diabetics with complications. They also found that there was an inverse relationship between serum Mg levels and glycated hemoglobin (HbA1c) in type 2 DM patients.

The relationship between Mg and Type 2 DM has been established and about a third of cases with Type 2 DM have hypomagnesemia.^[3]

Therefore, this study was conducted to see if there is any correlation between serum Mg and glycemic control in Type 2 DM patients.

Aim of the Study

The aim of the study was as follows:

- To evaluate serum Mg level in type 2 DM patients
- To see whether there is any correlation with HbA1c.

MATERIALS AND METHODS

A total of 50 cases and controls from medicine outpatient department were included in the study. The study was done after obtaining approval from the Institutional Ethics Committee.

Exclusion Criteria

Renal failure patients, Type I DM patients, chronic alcohol consumption, acute pancreatitis, patients on loop/thiazide diuretics or Mg supplement/Mg containing antacids, and any

other conditions causing low Mg levels were excluded from the study.

Sampling and Methods

Under aseptic precautions, 5 ml blood was collected from antecubital vein for serum Mg, fasting blood sugar (FBS), postprandial blood sugar (PPBS), and HbA1c after overnight fasting.

Mg was assayed in Siemens Advia Chemistry System. HbA1c analysis was done by ion exchange resin method.

The data were analyzed using Statistical Package for the Social Sciences and data recorded as mean \pm standard deviation and were considered significant when $P \leq 0.05$.

RESULTS

Out of total 50 patients, 36 were male and 14 cases were female, and most of cases were seen in the age group of 46–50 years. The Mean \pm SD of serum Mg in controls (males) was found to be 1.9 ± 0.16 mg/dl while mean \pm SD of serum Mg in cases (males) was found to be 1.61 ± 0.16 mg/dl. The mean and SD of serum Mg in controls (females) was found to be 1.93 ± 0.16 mg/dl while mean and SD of serum Mg in cases (females) was 1.67 ± 0.11 mg/dl. Serum Mg was found to be low in all age groups of both male and female cases. From this, we can infer that serum Mg is lower in cases than in controls [Table 1]. Levels of HbA1c significantly increase with the extent of DM, while the levels of serum Mg significantly decrease with the increase in time span of DM [Table 2].

The mean serum Mg in cases is 1.64 ± 0.15 mg/dl and mean serum Mg in controls is 1.9 ± 0.16 mg/dl. From Table 3, it is evident that the mean Mg level in cases is less than that in controls and it was found to be statistically very highly significant. Mean HbA1c in cases is $7.49 \pm 1.22\%$ and mean HbA1c in controls is $4.64 \pm 0.36\%$. From the above table, it can be seen that the mean HbA1c in cases is higher than that in controls and it was found to be statistically very highly significant.

Table 1: Serum Mg in controls and cases

Age group (in years)	Controls		Cases	
	Male (Mean \pm SD) mg/dl	Female (Mean \pm SD) mg/dl	Male (Mean \pm SD) mg/dl	Female (Mean \pm SD) mg/dl
40–45	2.00 \pm 0.18	2.10 \pm 0.21	1.66 \pm 0.19	1.70 \pm 0.10
46–50	1.97 \pm 0.13	1.97 \pm 0.13	1.61 \pm 0.18	1.67 \pm 0.04
51–55	2.00 \pm 0.13	1.93 \pm 0.12	1.62 \pm 0.17	1.64 \pm 0.15
56–60	1.78 \pm 0.06	1.80 \pm 0.00	1.58 \pm 0.10	1.70 \pm 0.00
>60	1.80 \pm 0.06	0	1.60 \pm 0.12	0
Total	1.90 \pm 0.16	1.93 \pm 0.16	1.61 \pm 0.16	1.67 \pm 0.11

Mg: Magnesium

Table 2: Serum Mg and HbA1c in cases with duration of DM

Duration of diabetes (in years)	Total number of cases	HbA1c (Mean±SD)%	Serum Mg (Mean±SD) mg/dl
≤1	7	6.20±0.27	1.73±0.28
2–5	20	7.19±0.98	1.60±0.18
6–10	22	8.19±1.16	1.59±0.13
>10	1	7.10±0.00	1.70±0.00
Total	50	7.49±1.22	1.64±0.15 mg/dl
		<i>P</i> <0.001	<i>P</i> <0.05

HbA1c: Glycated hemoglobin, DM: Diabetes mellitus, Mg: Magnesium

Table 3: Serum Mg and HbA1c in cases and controls

Age group (in years)	Serum Mg (mg/dl)			HbA1c (%)		
	Cases (Mean±SD)	Controls (Mean±SD)	“ <i>P</i> -value”	Cases (Mean±SD)	Controls (Mean±SD)	“ <i>P</i> -value”
40–45	1.69±0.17	2.01±0.21	<i>P</i> <0.01	6.50±0.77	4.48±0.31	<i>P</i> <0.001
46–50	1.63±0.17	1.97±0.14	<i>P</i> <0.001	7.41±1.36	4.50±0.21	<i>P</i> <0.001
51–55	1.58±0.15	1.97±0.18	<i>P</i> <0.001	7.59±0.88	4.50±0.24	<i>P</i> <0.001
56–60	1.60±0.11	1.78±0.06	<i>P</i> <0.001	8.07±0.93	5.02±0.22	<i>P</i> <0.001
>60	1.6±0.12	1.8±0.07	<i>P</i> <0.001	8.50±1.02	4.94±0.39	<i>P</i> <0.001
Total	1.64±0.15	1.9±0.16	–	7.49±1.22	4.64±0.36	–

HbA1c: Glycated hemoglobin, Mg: Magnesium

Table 4: Serum Mg and HbA1c in cases with duration of DM

Duration of diabetes (in years)	Total number of cases	HbA1c (Mean±SD)%	Serum Mg (Mean±SD) mg/dl
≤1	7	6.20±0.27	1.73±0.28
2–5	20	7.19±0.98	1.60±0.18
6–10	22	8.19±1.16	1.59±0.13
>10	1	7.10±0.00	1.70±0.00
Total	50	7.49±1.22%	1.64±0.15 mg/dl
		<i>P</i> <0.001	<i>P</i> <0.05

HbA1c: Glycated hemoglobin, DM: Diabetes mellitus, Mg: Magnesium

From Table 4, it can be seen that the levels of HbA1c very significantly increases with the increase in extent of DM, while the levels of serum Mg significantly decrease with the increase in time span of DM.

From Table 5, it is obvious that the mean FBS and PPBS in cases were found to be very significantly higher than that of controls. The mean HbA1c in cases was found to be very significantly higher than that in control.

DISCUSSION

Apart from being linked with type 2 diabetes, several studies have found a negative correlation between glycemic control and serum Mg levels.^[12-16] Different authors have different opinion about Mg in diabetes, some suggesting that diabetes in itself may cause hypomagnesemia, while many have reported that a high dietary intake of Mg may provide a role in reducing the risk of complications in Type 2 DM.^[17-20]

Table 5: Comparison of FBS, PPBS, and HbA1c

Parameters	Cases (Mean±SD)	Controls (Mean±SD)	“ <i>P</i> -value”
FBS	159.72±53.91 mg/dl	86.4±7.32 mg/dl	<i>P</i> <0.001
PPBS	230.66±92.93 mg/dl	118.5±17.68 mg/dl	<i>P</i> <0.001
HbA1c (%)	7.49±1.22	4.64±0.36	<i>P</i> <0.001

HbA1c: Glycated hemoglobin, FBS: Fasting blood sugar, PPBS: Postprandial blood sugar

There have also been studies which suggest that supplementation of oral Mg in type 2 diabetic patients improved their insulin sensitivity as well as metabolic control.^[21] It is still not very clear how hypomagnesemia induces or worsens existing diabetes. Magnesium besides being an essential activator of important enzymes in the body, has also a role in insulin's secretion, binding and activity.^[22-24] It was suggested that low serum Mg may lead to a defective transport of glucose and also cause an alteration in the post-receptorial signaling of insulin.^[6-9]

This study was conducted to assess serum Mg levels in type 2 DM patients and its relation with glycemic control. The study showed that serum Mg was notably lower in type 2 DM patients when compared to controls. Similar observations were also made by Razeena *et al.*^[25]

In this study, it was also seen that the HbA1c levels significantly increase with the increase of time span of DM ($P < 0.001$), while the levels of serum Mg significantly decrease with the increase in duration of DM ($P < 0.05$). Furthermore, with increased levels of HbA1c, it was observed that the serum Mg levels were significantly decreased ($P < 0.01$). Thus, our study suggests negative correlation between serum Mg and HbA1c.

Corsonello *et al.*^[26] and Corica *et al.*^[27] were in concordance with our study, they observed a negative correlation between serum ionized Mg levels and HbA1c and also found it to be statistically significant. They also remarked that serum ionized Mg decreases together with the increase in plasma HbA1c level. These findings may be due to the fact that their cases may be having incipient nephropathy or metabolic syndrome.

Verma *et al.*^[28] were of the same conclusion that with increase in time span of DM, HbA1c values show a significant increase ($P < 0.001$). However, Kabadi^[29] did not find any significant relationship between age of patients, duration of DM, FBS, and HbA1c. The study postulated that HbA1c concentrations in elderly populations may be related to associate chronic disorder rather than old age.

Masood *et al.*,^[30] Walter *et al.*,^[31] and Saeed *et al.*^[32] have observed serum Mg within normal range in both Type 2 diabetic patients and in healthy controls. They have postulated that their observations were because of exclusion of patients undergoing treatment with diuretics and patients of renal failure also that serum Mg and other trace elements status may be a consequence of DM or disturbances of this trace element may lead to further progression of the disease.

Small sample size and use of end point method for serum Mg estimation are the main limitations of the study. For a conclusive statement on Mg status, subsequent research with a large sample load and increased duration of study with ion selective electrode (ISE method) will give us a better evidence of the actual Mg status of the body and its clinical significance.

CONCLUSION

Serum Mg levels were significantly decreased when compared to controls and it was inversely correlated with HbA1c levels and also it significantly increases with the increase in time span of DM. Hypomagnesemia may be a

consequence of complications of DM or it may be a cause leading to the development of complications of DM.

REFERENCES

1. Sicree R, Shaw J, Zimmet P. The global burden. Diabetes and impaired glucose tolerance. Prevalence and projections. In: Gan D, editor. Diabetes Atlas. 3rd ed. Brussels: International Diabetes Federation; 2006. p. 16-103.
2. Burtis CA. Teitz Clinical Chemistry and Molecular Diagnostics. 4th ed. Philadelphia, PA: Saunders; 1912. p. 886.
3. Rude RK. Magnesium deficiency and diabetes mellitus. Causes and effects. Postgrad Med 1992;92:217-9, 222.
4. Saris NE, Mervaala E, Karppanen H, Khawaja JA, Lewenstam A. Magnesium. An update on physiological, clinical and analytical aspects. Clin Chim Acta 2000;294:1-26.
5. Wolf FI, Trapani V, Simonacci M, Ferré S, Maier JA. Magnesium deficiency and endothelial dysfunction: Is oxidative stress involved? Magnes Res 2008;21:58-64.
6. Dzurik R, Stetikova K, Spustova V, Fetkowska N. The role of magnesium deficiency in insulin resistance: An *in vitro* study. J Hypertens 1991;9 Suppl 6:S312-3.
7. Grafton G, Baxter MA. The role of magnesium in diabetes mellitus. J Diabetes Complications 1992;6:143-9.
8. Durlach J, Altura B, Altura BM. Highlights and summary of the 10th annual french colloquium on magnesium. Magnesium 1983;2:330-6.
9. Tonyai S, Motto C, Rayssiguer Y, Heaton FW. Erythrocyte membrane in magnesium deficiency. Am J Nutr 1985;4:399.
10. Sharma A, Dabla S, Agrawal RP, Barjatya H, Kochar DK, Kothari RP. Serum magnesium: An early predictor of course and complications of diabetes mellitus. J Indian Med Assoc 2007;105:16, 18, 20.
11. Ankush RD, Suryakar AN, Ankush NR. Hypomagnesemia in Type-2 diabetes mellitus patients: A study on the status of oxidative and nitrosative stress. Indian J Clin Biochem 2009;24:184-9.
12. Pham PC, Pham PM, 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;63:429-36.
13. Mather H, Nisbet JA, Burton GH, Poston GJ, Bland JM, Bailey PA, *et al.* Hypomagnesemia in diabetes. Clin Chim Acta 1979;95:235-42.
14. Pon KK, Ho PW. Subclinical hyponatremia, hyperkalemia and hypomagnesemia in patients with poorly controlled diabetes mellitus. Diabetes Res Clin Pract 1989;7:163-7.
15. Paolisso G, Sgambato S, Gambardella A, Pizza G, Tesaro P, Varricchio M, *et al.* Daily magnesium supplements improve glucose handling in elderly subjects. Am J Clin Nutr 1992;55:1161-7.
16. Resnick L, Altura BT, Gupta RK, Laragh JH, Alderman MH, Altura BM. Intracellular and extracellular magnesium depletion in Type 2 (non-insulin-independent) diabetes mellitus. Diabetologia 1993;36:767-70.
17. Kao WH, Folsom AR, Nieto J, Mo JP, Watson RL, Brancati FL. Serum and dietary magnesium and the risk for Type 2 diabetes mellitus. The atherosclerosis risk in communities study. Arch Intern Med 1999;159:2151-9.
18. Lopez-Ridaura R, Willett WC, Rimm EB, Liu S, Stampfer MJ,

- Manson JE, *et al.* Magnesium intake and risk of Type 2 diabetes in men and women. *Diabetes Care* 2004;27:134-40.
19. Song Y, Manson JE, Buring JE, Liu S. Dietary magnesium intake in relation to plasma insulin levels and risk of Type 2 diabetes in women. *Diabetes Care* 2004;27:59-65.
 20. 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 US black women. *Diabetes Care* 2006;29:2238-43.
 21. Rodriguez-Moran M, Guerrero-Romero F. Oral magnesium supplementation improves insulin sensitivity and metabolic control in Type 2 diabetic subjects. *Diabetes Care* 2003;26:1147-52.
 22. Rodriguez-Moran M, Mendia LE, Galvan GZ, Guerrero-Romero F. The role of magnesium in Type 2 diabetes: A brief based-clinical review. *Magnes Res* 2011;24:156-62.
 23. Kim DJ, Xun P, Liu K, Loria C, Yokota K, Jacobs DR Jr., *et al.* Magnesium intake in relation to systemic inflammation, insulin resistance, and the incidence of diabetes. *Diabetes Care* 2010;33:2604-10.
 24. Tosiello L. Hypomagnesemia and diabetes mellitus. A review of clinical implications. *Arch Intern Med* 1996;156:1143-8.
 25. Razeena KC, Maliakkal J, Nair G. Serum magnesium levels in Type 2 diabetes with metabolic syndrome. *Natl J Physiol Pharm Pharmacol* 2016;6:520-5.
 26. Corsonello A, Lentile R, Buemi N, Cucinotto D, Mauro VN, Macaione S, *et al.* Serum ionized magnesium in Type 2 diabetes with microalbuminuria or clinical proteinuria. *AMJ Nephrol* 2000;20:187-92.
 27. Corica F, Corsonello A, Lentile R, Cucinotta D, Di Benedetto A, Perticone F, *et al.* Serum ionized magnesium levels in relation to metabolic syndrome in Type 2 diabetic patients. *J Am Coll Nutr* 2006;25:210-5.
 28. Verma M, Paneri S, Badi P, Raman PG. Effect of increasing duration of diabetes mellitus Type 2 on glycated hemoglobin and insulin sensitivity Indian *J Clin Biochem* 2006;21:142-6.
 29. Kabadi UM. Glycosylation of proteins. Lack of influence on aging. *Diabetes Care* 1998;11:421-32.
 30. Masood N, Baloch GH, Ghori RA, Memon IA, Memon MA, Memon MS. Serum zinc and magnesium in Type 2 diabetic patients. *J Coll Physicians Surg Pak* 2009;19:483-6.
 31. Walter RM Jr., Uriu-Hare JY, Olin KL, Oster MH, Anawalt BD, Critchfield JW, *et al.* Copper, zinc, manganese, and magnesium status and complications of diabetes mellitus. *Diabetes Care* 1991;14:1050-6.
 32. Saeed H, Haj S, Qasim B. Estimation of magnesium level in Type 2 diabetes mellitus and its correlation with HbA1c level. *Endocrinol Diab Metab* 2019;2:e48.

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