Section: Miscellaneous

Original Research Article

CORRELATION OF SERUM MAGNESIUM IN DIABETIC PATIENTS WITH PROTEINURIA

Sanket Patil G.[1], Sharanabasavaraj Devareddy[2]

[1]Assistant Professor, Raichur Institute of Medical Sciences, Raichur, India.
[2]Senior Resident, Siddhartha Institute of Medical Sciences, T. Begur, India.

Received : 09/08/2025
Received in revised form : 27/09/2025
Accepted : 14/10/2025

Keywords:
Magnesium, diabetes mellitus, proteinuria, diabetic nephropathy, HbA1c, lipid profile.

Corresponding Author:
Dr. Sanket Patil G,
Email: sanketpatilg07071989@gmail.com

DOI: 10.47009/jamp.2025.7.6.203

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

Int J Acad Med Pharm
2025; 7 (6); 1092-1096

ABSTRACT

Background: Magnesium is the second most important intracellular cation, acting as a cofactor in over 300 enzymatic reactions involving energy metabolism and nucleic acid synthesis.[1] Hypomagnesemia occurs in 25–39% of diabetic patients due to poor oral intake, impaired gastrointestinal absorption, and enhanced renal magnesium excretion, particularly when proteinuria is present.[2,3] An inverse correlation exists between serum magnesium levels and proteinuria in diabetic nephropathy. **Objective:** To study the correlation of serum magnesium in diabetic patients with proteinuria and assess its relationship with glycemic control, lipid profile, and renal function. **Materials and Methods:** This observational study included 50 diabetic patients (12 type 1, 38 type 2) admitted or attending the general medicine department at RIMS, Raichur, between July and December 2012. Serum magnesium, 24-hour urinary protein, fasting blood glucose, HbA1c, serum creatinine, and lipid profile were measured. Pearson correlation analysis was performed using SPSS version 15. **Result:** Of 50 patients, 25 had microalbuminuria and 25 had macroalbuminuria. Mean diabetes duration was 13.2 years, mean serum magnesium 1.59 mg/dl, and mean 24-hour urinary protein 467.26 mg. Serum magnesium showed strong inverse correlations with duration of diabetes ($r = –0.88$, $p<0.001$), fasting blood sugar ($r = –0.72$, $p<0.001$), HbA1c ($r = –0.86$, $p<0.001$), total cholesterol, LDL cholesterol, triglycerides, serum creatinine, and 24-hour urinary protein ($r = –0.87$, $p<0.001$). A positive correlation was observed with HDL cholesterol ($r = 0.82$, $p<0.001$). Patients with macroalbuminuria had significantly lower serum magnesium than those with microalbuminuria. **Conclusion:** This study demonstrates a significant inverse correlation between serum magnesium and proteinuria severity. Routine assessment of serum magnesium in diabetic patients, combined with oral supplementation, may improve glycemic control and potentially reduce progression of renal and vascular complications.

INTRODUCTION

Magnesium is the fourth most common cation in the body and the second most abundant intracellular cation after potassium.[1] It acts as a cofactor in more than 300 enzymatic reactions involving energy metabolism, nucleic acid synthesis, and glucose homeostasis.[2] Less than 1% of total body magnesium is found in serum and red blood cells, with 53% located in bone, 27% in muscle, and 19% in soft tissue.[3]

Diabetes mellitus has reached epidemic proportions worldwide, with India harboring the largest population of diabetic patients. The International Diabetes Federation reported approximately 40.9 million diabetic patients in India in 2006, with projections of 69.9 million by 2025.[4] A Chennai study showed diabetes prevalence increased significantly by 72.3% within 14 years.[5] Diabetic nephropathy develops in approximately one-third of diabetic patients, and in India, it is expected to develop in 6.6 million people out of 30 million with diabetes.[6] Studies in south India have shown microalbuminuria prevalence of 26.9% and overt proteinuria of 2.2%.[7]

Hypomagnesemia in diabetic patients results from poor oral intake, poor gastrointestinal absorption, and enhanced renal magnesium excretion.[8] Hyperglycemia-induced osmotic diuresis, metabolic acidosis, and hypoalbuminemia further increase the ultrafilterable magnesium load.[8] Importantly, microalbuminuria and overt proteinuria contribute significantly to renal magnesium wasting due to protein-bound magnesium loss.[8]

Magnesium plays crucial roles in glucose homeostasis by affecting insulin secretion and glucose uptake by cells. Magnesium deficiency inhibits the acute phase of insulin release in response to glucose challenge and is associated with insulin

ISSN (O): 2687-5365; ISSN (P): 2753-6556

resistance; conversely, insulin resistance is associated with low serum magnesium.[9] An inverse correlation exists between serum magnesium and serum cholesterol, triglycerides, and low-density lipoprotein levels.[10] Magnesium deficiency increases angiotensin II-induced plasma aldosterone concentration and production of thromboxane and vasoconstrictor prostaglandins, leading to increased vascular tone and progression of atherosclerosis.[11] Thus, hypomagnesemia is implicated in both metabolic and vascular complications of diabetes.[12]

The mechanism by which increased proteinuria leads to further magnesium wasting involves excessive tubular reabsorption of proteins, accumulating in tubular epithelial cells and releasing vasoactive and inflammatory cytokines. This leads to overexpression of pro-inflammatory and fibrotic cytokines, causing tubulointerstitial injury and ultimately renal scarring and failure.[13]

Limited data exist regarding the correlation between serum magnesium and proteinuria in Indian diabetic populations. This study was designed to evaluate this relationship and its association with glycemic control, lipid profile, and renal function parameters in a hospital-based cohort.

MATERIALS AND METHODS

Study Design and Setting

This observational study was conducted at Raichur Institute of Medical Sciences, from July 20023 to December 2023. The study protocol was approved by the Institutional Ethical Committee.

Study Population

Patients were recruited from those admitted to the general medical ward for diabetes control and those attending the general medicine outpatient department. The inclusion criteria were: (1) Type 2 diabetes mellitus of any duration, and (2) Type 1 diabetes mellitus of more than 5 years duration.

Exclusion criteria were: systemic hypertension, congestive cardiac failure, urinary tract infection, severe diarrhea, chronic alcoholism, diabetic ketoacidosis, total parenteral nutrition, and use of drugs known to cause hypomagnesemia (loop/thiazide diuretics, cisplatin, cyclosporine, aminoglycosides, amphotericin B).

Clinical and Laboratory Evaluation

Detailed clinical profiles including age, sex, duration of diabetes, relevant comorbidities, and medication history were documented. A 2–5 ml blood sample was drawn from each patient and allowed to clot. Serum was separated by centrifugation and stored for analysis. Laboratory measurements included:

- Serum magnesium: Estimated using a colorimetric method
- Glycemic control: Fasting and post-prandial blood glucose, HbA1c
- Lipid profile: Total cholesterol, HDL cholesterol, LDL cholesterol, triglycerides
- Renal function: Serum creatinine
- Proteinuria: 24-hour urinary protein

Proteinuria was classified as microalbuminuria (30–299 mg/24 hours) and macroalbuminuria (≥300 mg/24 hours).

Statistical Analysis

Statistical analysis was performed using R software. Descriptive statistics (mean, range, standard deviation) were calculated for all variables. Pearson correlation coefficients were computed to assess relationships between serum magnesium and other variables including duration of diabetes, glycemic parameters, lipid profile components, serum creatinine, and 24-hour urinary protein. A p-value <0.05 was considered statistically significant.

RESULTS

Patient Demographics and Clinical Characteristics

A total of 50 diabetic patients were enrolled: 12 (24%) with type 1 diabetes and 38 (76%) with type 2 diabetes. Among type 1 diabetics, 9 patients had microalbuminuria and 3 had macroalbuminuria. In type 2 diabetics, 16 patients had microalbuminuria and 22 had macroalbuminuria, indicating a higher burden of overt nephropathy in type 2 disease.

Mean age of the cohort was 52.8 ± 14.99 years. Mean diabetes duration was 13.20 ± 4.27 years. Mean fasting blood glucose was 184.74 ± 34.72 mg/dl, post-prandial glucose 250.68 ± 43.68 mg/dl, and HbA1c 7.70 ± 0.75%. Mean serum magnesium was 1.592 ± 0.121 mg/dl, with a range of 1.4–1.8 mg/dl. Mean 24-hour urinary protein was 467.26 ± 368.17 mg, with a range of 56–1698 mg.

Lipid profile parameters showed: HDL cholesterol 43.08 ± 9.15 mg/dl, LDL cholesterol 153.68 ± 51.96 mg/dl, total cholesterol 222.78 ± 14.06 mg/dl, and triglycerides 216.08 ± 34.46 mg/dl. Mean serum creatinine was 1.150 ± 0.27 mg/dl.

Correlation of Serum Magnesium with Glycemic Parameters and Disease Duration

Serum magnesium showed a strong inverse correlation with duration of diabetes ($r = –0.882$, $p<0.001$), indicating that longer diabetes duration was associated with lower magnesium levels. Similarly, fasting blood sugar correlated inversely with serum magnesium ($r = –0.720$, $p<0.001$), and HbA1c showed a strong negative correlation ($r = –0.861$, $p<0.001$). These findings indicate that poor glycemic control is closely associated with hypomagnesemia.

Correlation of Serum Magnesium with Lipid Profile

Serum magnesium demonstrated a positive correlation with HDL cholesterol ($r = 0.820$, $p<0.001$), showing that higher magnesium levels were associated with higher protective HDL cholesterol. Conversely, serum magnesium showed strong inverse correlations with LDL cholesterol ($r = –0.866$, $p<0.001$), total cholesterol ($r = –0.621$, $p<0.001$), and triglycerides ($r = –0.847$, $p<0.001$).

ISSN (O): 2687-5365; ISSN (P): 2753-6556

These results indicate that patients with hypomagnesemia exhibit an atherogenic lipid profile characterized by elevated LDL and triglycerides and reduced HDL cholesterol.

Correlation of Serum Magnesium with Proteinuria and Renal Function

The most significant finding was the strong inverse correlation between serum magnesium and 24-hour urinary protein ($r = –0.869$, $p<0.001$), demonstrating that higher proteinuria was accompanied by lower serum magnesium levels. Serum magnesium also showed an inverse correlation with serum creatinine ($p<0.001$), indicating deteriorating renal function in patients with hypomagnesemia.

Patients with macroalbuminuria (≥300 mg/24 hours) had significantly lower mean serum magnesium levels compared to those with microalbuminuria (30–299 mg/24 hours). Additionally, duration of diabetes correlated positively with 24-hour urinary protein ($r = 0.836$, $p<0.001$), with macroalbuminuria typically emerging beyond a mean diabetes duration of approximately 13 years.

Table 1: Clinical and laboratory profile of diabetic patients (N = 50)

Variable	Mean ± SD (range)
Age (years)	52.8 ± 14.99
Duration of diabetes (years)	13.20 ± 4.27
Diabetes type	Type 1: 12 (24%); Type 2: 38 (76%)
Albuminuria category	Microalbuminuria: 25; Macroalbuminuria: 25
Type 1 DM albuminuria	Micro: 9; Macro: 3
Type 2 DM albuminuria	Micro: 16; Macro: 22
Fasting blood glucose (mg/dl)	184.74 ± 34.72
Post-prandial glucose (mg/dl)	250.68 ± 43.68
HbA1c (%)	7.70 ± 0.75
Serum magnesium (mg/dl)	1.592 ± 0.121 (1.4–1.8)
24-hour urinary protein (mg/24 h)	467.26 ± 368.17 (56–1698)
HDL cholesterol (mg/dl)	43.08 ± 9.15
LDL cholesterol (mg/dl)	153.68 ± 51.96
Total cholesterol (mg/dl)	222.78 ± 14.06
Triglycerides (mg/dl)	216.08 ± 34.46
Serum creatinine (mg/dl)	1.150 ± 0.27

Table 2: Correlation of serum magnesium with clinical and biochemical variables (N = 50)

Variable	Correlation with serum Mg (r)	p value
Duration of diabetes (years)	–0.882	<0.001
Fasting blood glucose (mg/dl)	–0.720	<0.001
HbA1c (%)	–0.861	<0.001
Total cholesterol (mg/dl)	–0.621	<0.001
LDL cholesterol (mg/dl)	–0.866	<0.001
Triglycerides (mg/dl)	–0.847	<0.001
HDL cholesterol (mg/dl)	0.820	<0.001
24-hour urinary protein (mg/24 h)	–0.869	<0.001
Serum creatinine (mg/dl)	Inverse (r, p not fully given)	<0.001

DISCUSSION

This study of 50 diabetic patients demonstrates a strong and consistent inverse relationship between serum magnesium levels and multiple markers of poor glycemic control, atherogenic dyslipidemia, and advanced diabetic nephropathy.

The inverse correlation between serum magnesium and duration of diabetes, fasting blood glucose, and HbA1c aligns with previous reports. Schlinger et al. demonstrated significantly reduced magnesium levels in patients with poor glycemic control.[14] The mechanism underlying this relationship is well-established: magnesium serves as a critical cofactor for the Na/K-ATPase pump and enzymes involved in glucose transport and phosphorylation.[15] Magnesium deficiency impairs insulin receptor tyrosine kinase activity, promoting insulin resistance and perpetuating hyperglycemia. Intracellular magnesium depletion reduces the activity of enzymes requiring high-energy phosphate bonds, further worsening insulin action. This creates a vicious cycle where insulin resistance reduces magnesium uptake in insulin-sensitive tissues, leading to further intracellular magnesium depletion.[16]

The significant associations between low magnesium and elevated LDL cholesterol, triglycerides, and total cholesterol, combined with reduced HDL cholesterol, are consistent with experimental evidence. Magnesium modulates HMG-CoA reductase, the rate-limiting enzyme in cholesterol metabolism, and regulates lipoprotein lipase activity.[17] Magnesium deficiency impairs both enzymes, leading to elevated LDL and triglycerides and reduced HDL. The atherogenic lipid profile observed in hypomagnesemic patients likely accelerates atherosclerosis and increases cardiovascular mortality risk in diabetic populations.[18]

The central finding of this study—the strong inverse correlation between serum magnesium and 24-hour urinary protein—is noteworthy and clinically significant. This relationship supports magnesium's role in preventing or slowing progression of diabetic nephropathy. Corsonello et al. demonstrated

ISSN (O): 2687-5365; ISSN (P): 2753-6556

significantly lower serum magnesium in diabetic patients with micro- or macroalbuminuria and showed a rapid decline in renal function associated with lower magnesium.[19] Our study extends these observations to an Indian cohort and provides quantitative evidence of this relationship.

The mechanism underlying the magnesium-proteinuria relationship is multifaceted. Hyperglycemia promotes non-enzymatic glycation of proteins, forming advanced glycation end products (AGEs) that accumulate in glomeruli and tubules, causing mesangial expansion, glomerular basement membrane thickening, and proteinuria.[20] Proteinuria itself drives further complications by causing excessive tubular reabsorption and accumulation of proteins in tubular epithelial cells, which release inflammatory cytokines including transforming growth factor-β and monocyte chemoattractant protein-1.[21] These mediators promote pro-inflammatory and fibrotic cascades, leading to tubulointerstitial fibrosis and renal scarring.[22]

Magnesium acts as a natural calcium antagonist and modulates intracellular calcium flux. Magnesium deficiency increases intracellular calcium concentration, activating protein kinase C and mitogen-activated protein kinases (MAPKs), which stimulate synthesis and deposition of extracellular matrix components.[23] Additionally, magnesium maintains the function of Na/K-ATPase and enhances inositol transporter affinity; magnesium deficiency causes inositol depletion, reducing activity of regulatory proteins and worsening diabetic nephropathy.[24]

Furthermore, magnesium deficiency impairs the balance of vasoactive and hemostatic mediators. Low magnesium increases synthesis of thromboxane A2 and vasoconstrictor prostaglandins while reducing vasodilatory prostacyclin production.[25] This hemostatic shift increases glomerular filtration pressure and basal membrane damage, reducing glomerular filtration rate and promoting proteinuria progression.

The strong positive correlation between diabetes duration and proteinuria, with macroalbuminuria typically appearing at approximately 13 years, aligns with the natural history of diabetic nephropathy described in type 1 diabetes, where 40% develop microalbuminuria by 5–10 years, and approximately 50% progress to macroalbuminuria within 7–10 years of microalbuminuria onset.[26]

Clinical Implications

Oral magnesium supplementation has been shown to improve insulin secretion and increase insulin sensitivity by approximately 10%, with blood glucose reduction of 37% in some studies>[27] Studies have also shown that magnesium supplementation reduces platelet aggregation by decreasing thromboxane A2 levels,[28] reduces low-density lipoprotein and cholesterol,[29] and produces moderate decreases in systolic blood pressure.[30] These effects suggest potential renoprotective and cardioprotective benefits in diabetic patients.

Limitations

This study has several limitations. The sample size of 50 patients is modest; larger studies are needed to confirm these findings in diverse populations. The assessment of renal function relied solely on serum creatinine rather than estimated glomerular filtration rate (eGFR), which would provide more accurate assessment of glomerular filtration. Cross-sectional design prevents causality determination. The study was conducted in a single institution, potentially limiting generalizability.

CONCLUSION

This observational study demonstrates strong and clinically significant correlations between serum magnesium and multiple markers of diabetic disease severity:

1. A significant inverse correlation exists between serum magnesium levels and proteinuria severity, with patients having macroalbuminuria showing the lowest magnesium levels.
2. Serum magnesium correlates inversely with diabetes duration, indicating progressively worsening magnesium deficiency over disease course.
3. Poor glycemic control (high fasting blood sugar and HbA1c) is strongly associated with reduced serum magnesium levels.
4. An atherogenic lipid profile (elevated total cholesterol, LDL cholesterol, triglycerides, and reduced HDL cholesterol) is closely associated with hypomagnesemia.
5. Declining renal function (elevated serum creatinine) is associated with lower serum magnesium levels.
6. Diabetes duration correlates positively with proteinuria magnitude, with overt proteinuria typically emerging beyond 13 years of diabetes.

These findings establish serum magnesium as a useful biomarker of metabolic and renal disease severity in diabetes. Given the emerging evidence that magnesium deficiency is implicated in multiple complications of diabetes including poor glycemic control, dyslipidemia, hypertension, and progressive nephropathy, routine assessment of serum magnesium in diabetic patients is warranted. Oral magnesium supplementation, combined with optimal glycemic and blood pressure control, may improve metabolic parameters and potentially slow the progression of renal and vascular complications. Further prospective randomized controlled trials are needed to establish optimal magnesium supplementation regimens and to confirm clinical benefits in reducing morbidity and mortality from diabetic complications.

REFERENCES

1. Reinhart RA. Magnesium metabolism: A review with special reference to the relationship between intracellular content and serum levels. Arch Intern Med. 1988;148:2415–2420.

ISSN (O): 2687-5365; ISSN (P): 2753-6556

2. Elin RJ. Magnesium: the fifth but forgotten electrolyte. Am J Clin Pathol. 1994;102:616–622.
3. Shils ME. Magnesium. In: Shils ME, Olson JE, Shike M, Ross AC, editors. Modern Nutrition in Health and Disease. Baltimore: Williams & Wilkins; 1998. p. 169–192.
4. Sicree R, Shaw J, Zimmet P. Diabetes and impaired glucose tolerance. In: Gan D, editor. Diabetes Atlas. 3rd ed. Belgium: International Diabetes Federation; 2006. p. 15–103.
5. Mohan V, Deepa M, Deepa R, et al. Secular trends in the prevalence of diabetes and glucose tolerance in urban South India—the Chennai Urban Rural Epidemiology Study (CURES-17). Diabetologia. 2006;49:1175–1178.
6. [6] Hossain P, Kawar B, El Nahas M. Obesity and diabetes in the developing world—a growing challenge. N Engl J Med. 2007;356:213–215.
7. Unnikrishnan R, Rema M, Pradeepa R, et al. Prevalence and risk factors of diabetic nephropathy in an urban South Indian population—the Chennai Urban Rural Epidemiology Study (CURES 45). Diabetes Care. 2007;30:2108–2114.
8. Sjogren A, Floren CH, Nilsson A. Magnesium, potassium and zinc deficiency in subjects with type II diabetes mellitus. Acta Med Scand. 1988;224:461–466.
9. Hua H, Gonzales J, Rude RK. Magnesium transport induced ex vivo by a pharmacological dose of insulin is impaired in non-insulin-dependent diabetes mellitus. Magnes Res. 1995;8:359–366.
10. American Journal of Nephrology. 2000;20:187–192.
11. Nadler JL, Buchanan T, Natarajan R, et al. Magnesium deficiency produces insulin resistance and increased thromboxane synthesis. Hypertension. 1993;21:1024–1029.
12. Clinical Nephrology. 2005;63:429–436.
13. Graphton G, Bunce CM, Sheppard MC, et al. Effect of Mg2+ on Na+-dependent inositol transport: Role for Mg2+ in etiology of diabetic complications. Diabetes. 1992;41:35–39.
14. Schlingler et al. [Referenced for glycemic control and magnesium relationship].
15. Paolisso G, Scheen A, Cozzolino D, et al. Changes in glucose turnover parameters and improvement of glucose oxidation after 4-week magnesium administration in elderly noninsulin-dependent (type II) diabetic patients. J Clin Endocrinol Metab. 1994;78:1510–1514.
16. Rosolova H, Mayer O Jr, Reaven G. Effect of variations in plasma magnesium concentrations on resistance to insulin-mediated glucose disposal in nondiabetic subjects. J Clin Endocrinol Metab. 1997;82:3783–3785.
17. Lal J, Vasudev K, Kela AK, et al. Effect of oral magnesium supplementation on the lipid profile and blood glucose of patients with type 2 diabetes mellitus. J Assoc Physicians India. 2003;51:37–42.
18. Nadler JL, Malayan S, Luong H, et al. Intracellular free magnesium deficiency plays a key role in increased platelet reactivity in type II diabetes mellitus. Diabetes Care. 1992;15:835–841.
19. Corsonello A et al. Magnesium and vascular changes in hypertension. International Journal of Hypertension. 2012.
20. Formation of advanced glycation end products in diabetes: pathophysiology and clinical implications [Referenced from dissertation literature review].
21. Proteinuria-induced inflammatory cytokine release and tubulointerstitial fibrosis in diabetic nephropathy [Referenced from dissertation].
22. Endothelin and transforming growth factor-β in progression of diabetic renal disease [Referenced from dissertation].
23. Protein kinase C activation and extracellular matrix deposition in diabetic nephropathy [Referenced from dissertation].
24. Paolisso G, Tirelli A, Coppola L, et al. Magnesium administration reduces platelet hyperaggregation in NIDDM. Diabetes Care. 1989;12:167–168.
25. Thromboxane A2 and prostaglandin synthesis in magnesium deficiency [Referenced from dissertation].
26. Natural history and clinical manifestation of diabetic nephropathy [Referenced from dissertation literature review].
27. Supplementation studies demonstrating magnesium effects on insulin and glucose metabolism [Referenced from dissertation].
28. Nadler JL, Buchanan T, Natarajan R, et al. Magnesium deficiency produces insulin resistance and increased thromboxane synthesis. Hypertension. 1993;21:1024–1029.
29. Effects of magnesium supplementation on lipid profile in diabetic patients [Referenced from dissertation].
30. Purvis JR, Cummings DM, Landsman P, et al. Effect of oral magnesium supplementation on selected cardiovascular risk factors in noninsulin-dependent diabetics. Arch Fam Med. 1994;3:503–508.

ISSN (O): 2687-5365; ISSN (P): 2753-6556