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Serum Magnesium Useful for Early Detection and Progression of Type 2 Diabetes Mellitus and Nephropathy

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KEYWORDS:

Magnesium, Insulin, Type 2 Diabetes Mellitus and Nephropathy

ABSTRACT:

Introduction: : Magnesium, Insulin, urinary ACR, eGFR, play various roles in the pathophysiology of type 2 diabetes mellitus and nephropathy. This study aimed at determining whether serum magnesium, insulin, urinary ACR and eGFR are significantly altered during normo albuminuria of type 2 diabetes patients that subsequently develop micro and macro albuminuria and whether such changes are useful in predicting the disease early.

Objectives: To estimate serum magnesium and corelate with clinical markers of nephropathy in patients with type 2 diabetes mellitus. Additionally, the serum magnesium can serve has a early diagnostic and prognostic marker for nephropathy.

Methods: This was a cross sectional study which compared biochemical, clinical parameters in 40 type 2 diabetes mellitus with normo albuminuria, 40 type 2 diabetes mellitus with micro albuminuria, 40 type 2 diabetes mellitus with macro albuminuria and 40 age, gender and BMI matched healthy controls. Blood sugars, glycated haemoglobin, renal function tests, serum insulin, magnesium, eGFR and urinary ACR were analysed.

Results: There were significant differences in serum magnesium, insulin, urinary ACR, and eGFR among different stages of type 2 diabetes mellitus patients when compared to controls. Additionally, the serum magnesium negatively correlated with BMI, blood sugars, glycated haemoglobin, urea, creatinine, insulin, urinary ACR and positively correlated with eGFR (P=0.001**). Furthermore, the receiver operating characteristic curve analysis area uncer the curve for serum magnesium, urinary ACR and eGFR were; 0.989, 0.573 and 0.565 respectively. Decreased serum magnesium (specificity: 100; sensitivity; 95; CI=0.935 to 1.000; p=0.0001) were associated with T2DM and nephropathy.

Conclusions: Hypomagnesemia precede type 2 diabetes mellitus and can serve as early predictive and prognostic indices for type 2 diabetic nephropathy.

1. Introduction

Type 2 diabetes mellitus (T2DM) is a metabolic disease due to hyperglycemia and this is increasing in worldwide particularly in developing nations (1). The prevalence of T2DM in worldwide around 463 million people effected in 2029 and it will enhance up to 700 million by the year 2030 (2). The genetic history, food habits, metabolic and environmental factors contribute to enhances the blood sugars results hyperglycemia (3). The diabetic nephropathy (DN) is a clinical condition in patients with T2DM. The first clinical indicator of DN is microalbuminuria. The microalbuminuria might be linked to poor control of glucose levels and decreased antioxidants (4-5).

Magnesium is an essential mineral required for many biological activities like activation of enzymes, anti-oxidant and anti-inflammatory properties (6-7). The tyrosine kinase is phosphorylated enzyme involved in activation of insulin by phosphorylation; this reaction takes place with the presence of magnesium (8). Magnesium works as an antioxidant in the mitochondria. As an antioxidant, it helps prevent against damage caused by reactive oxygen bodies phosphate and may lower the incidence of renal disorders (9). It helps to

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reduce inflammation by suppressing inflammatory signalling pathways and reduce the generation of pro-inflammatory cytokines. Additionally, it involves enhances in endothelial function, tubular integrity, and renal function (10).

The recent studies reported decreased serum magnesium leads to impaired insulin secretion and activation results impaired cell uptake of glucose leads to hyperglycemia and T2DM. Along with that some of the studies reported that there was a significant relation between magnesium and elevated levels of microalbumin in patients with T2DM (11-13). The impact of magnesium insufficiency in diabetic patients on preventing renal problems remains unclear despite a plethora of research in this area. In order to evaluate the relationship between serum magnesium levels and microalbuminuria in type 2 diabetes mellitus patients.

2. Objectives

To estimate serum magnesium and corelate with clinical markers of nephropathy in patients with type 2 diabetes mellitus. Additionally, the serum magnesium can serve has a early diagnostic and prognostic marker for nephropathy.

3. Methods

This cross sectional analytical study conducted in department of biochemistry collaborated with general medicine at Raichur Institute of Medical Sciences, Raichur, Karnataka. In this study we recruited 160 participants; among these 120 were T2DM patients and 40 age and gender matched healthy controls considered as Group 1. The T2DM subjects were further sub grouped based on their microalbumin levels shown in figure 1 & Table 1.This cross sectional analytical study conducted after obtained approval from Institutional Ethics Committee and the study participants were recruited after taken informed concern forms.

Sample collection

Five (5) millilitres of overnight fasting sample collected from all the participants, 1 mL transferred to fluoride tube, 1 mL transferred to ethylene diamine tetra acetic acid and remaining 3 mL transferred to serum separation tube. The plasma and serum separated by centrifugation process. Along with blood sample spot fasting urine sample also collected and separated by centrifugation. All the separated samples were transferred into properly labelled aliquots until analysis was done.

The anthropometric and demographic data was collected from all the participants. The fasting blood sugar (FBS), serum urea, serum creatinine, was measured by laboratory standard methods. The glycated haemoglobin (HbA1c) was measured by high performance liquid chromatography, serum magnesium was analysed by calmigite indicator method. The microalbumin determined by immunoturbidimetry method. The serum insulin was determined by enzyme linked immunosorbent assay. The estimated glomerular filtration (eGFR) was calculated by modification of diet in renal diseases formula.

Statistical analysis

The data distribution was done by Kolmogorov smrinov (KS) test. The comparison between the groups done by analysis of variance, the correlation between the variables was done by pearson's correlation analysis. The receivers operating characteristic curve analysis is used to assess the diagnostic accuracy, sensitive and specificity of magnesium, eGFR and microalbumin between the T2DM patients with Normoalbuminuria and healthy controls. The statistical analysis done by using statistical package for the social sciences (SPSS) version 20.0.

4. Results

The base line characteristics of variables of the study participants shown in table 2. The age shown significance between the controls and T2DM patients (P=0.001**). The T2DM patients has significant increased BMI, FBS, HbA1c, serum urea, serum creatinine when compared to controls (P=0.001**). The serum insulin and urinary ACR significantly increased in T2DM patients when compared to controls (P=0.001**). The T2DM patients shown significantly decreased eGFR and serum magnesium when compared to controls (P=0.001**).

The comparison of variables between of the study subjects shown in table 3. The age shown significance between the study subjects (P=0.001**). There was a significant and drastically enhanced BMI, FBS, HbA1c, serum urea, serum creatinine levels in T2DM patients with normo, micro and macro albuminuria patients when compared to controls (P=0.001**). The T2DM patients

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with macro albuminuria shown significant highest levels of serum insulin and urinary ACR when compared to T2DM patients with micro, normoalbuminuria and controls (P=0.001**). There was a significantly decreased eGFR and serum magnesium in T2DM patients with normo, micro and macro albuminuria patients when compared to controls (P=0.001**).

The table 4 illustrates correlation of serum magnesium with biochemical and clinical parameters of the study. There was a significant negative correlation between serum magnesium and BMI, FBS, HbA1c, urea, creatinine, insulin (P=0.001**). Additionally, the serum magnesium positively correlated with eGFR (P=0.001**).

The table 5 illustrates that the receivers operating characteristics between urinary ACR, eGFR and serum magnesium in T2DM patients with normoalbuminuria and controls. The ROC curve analysis revealed the serum magnesium shown very high significant at AUC but the sensitivity 95 % and specificity 100 % (P=0.001**). The urinary ACR and eGFR not shown any significant at AUC the sensitivity (32 & 95 %) and specificity (47 & 70 %) (P=0.262 & 0.315).

The figure 2 shows the eGFR significantly reduced T2DM patients with macro, micro albuminuria when compared to T2DM with normoalbuminuria and controls. The urinary ACR drastically elevated in T2DM patients with normo, micro and macroalbuminuria when compared to controls. The serum magnesium was significantly decreased in T2DM with normo, micro and macroalbuminuria when compared to controls.

The figure 3 shows the scatter plots between serum magnesium and FBS, HbA1c, Insulin, urinary ACR and eGFR. The scatter plots shown that the serum magnesium negatively correlated with FBS, HbA1c, urinary ACR, insulin and positively correlated with eGFR.

5. Discussion

Nephropathy is a severe clinical condition in T2DM patients. Globally, Around 30 to 40 % of T2DM patients will affect with nephropathy (16). The microalbumin is a gold standard marker for diagnosis of nephropathy. The advanced studies reported that the microalbumin has lot of flows such as many T2DM patients with microalbumin revert back to Normoalbuminuria, the T2DM patients with Normoalbuminuria shown advanced renal pathology and also it will elevated in other diseases (17-19). There is a need for sensitive, specific and early detection of T2DM and nephropathy.

Magnesium (Mg) is the fourth most prevalent mineral and the most abundant intracellular cation in the human body (20). It has several vital functions, such as protein synthesis, antioxidant and utilized to prevent and cure a wide range of illnesses (21). The phosphorylated insulin will activates the glucose transporters results glucose uptake into the cells. The phosphorylation of insulin required magnesium, in the insulin receptors. There is a significant relationship is there between magnesium and insulin resistance and T2DM (22-23).

The recent studies also reported hypomagnesemia and these levels was negatively correlated with hyperglycemia in patients with T2DM then controls (24-26). Similarly, the present study observed significant and drastically decreased levels of serum magnesium in T2DM patients with normo, micro and macro albuminuria when compared to controls (P=0.001**) (Table 3). Along with that we also observed hypomagnesemia positively correlated with urinary ACR and negatively correlated with eGFR (P=0.001**) (Table 4).

Additionally, in our study the ROC curve analysis revealed that the serum magnesium has highest significant at AUC (p=0.0001**), the specificity (100) and sensitivity (95) then the urinary ACR and eGFR specificity (95 & 70) and sensitivity (32 & 47) (P=0.262 & 0.315). Based on the study findings the serum magnesium significantly decreased and positively correlated with hyperglycemia, urinary ACR and negatively correlated with eGFR in T2DM patients. The significant reduced levels of serum magnesium has direct relation in pathophysiology of T2DM and nephropathy (27-28). The measurement serum magnesium identify the T2DM and its complications.

6. Conclusion

The present study concludes that the serum magnesium can be used as early diagnostic and prognostic marker for type 2 diabetes mellitus and nephropathy.

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References

1. Rezaei M, Khazaei R, Mohaqiq Z, Raeesi V, Farkhondeh T, Samarghandian S. Effect of Magnesium Status on Microalbuminuria in Type 2 Diabetic Patients. Cardiovasc Hematol Agents Med Chem. 2023;21(1):55-59.
2. Kachhawa K, Kachhawa P, Agrawal D, Kumar S, Sarkar PD. Effects and association of pro-oxidants with magnesium in patients with diabetic nephropathy. Saudi J Kidney Dis Transpl. 2019 Sep-Oct;30(5):1032-1037.
3. Batar PK. Study of Serum Magnesium Level in Diabetes Mellitus and it's Correlation with Micro and Macro Complications. J Assoc Physicians India. 2022 Apr;70(4):11-12.
4. Pulido-Perez P, Pondigo-de JA, Hernandez-Hernandez ME, Torres-Rasgado E, Romero JR. Renal function, serum magnesium levels and mortality in COVID-19 patients with type 2 diabetes. Magnes Res. 2021 Feb 1;34(1):20-31.
5. Qamar S, Anwar M, Haroon ZH, Bibi A, Munir MU, Kirmani SI. Evaluation of hypomagnesaemia in diabetic patients with nephropathy in a reference clinical laboratory: A comparative cross sectional study. J Pak Med Assoc. 2023 Apr;73(4):869-871.
6. Corsonello A, Ientile R, Buemi M, Cucinotta D, Mauro VN, Macaione S, Corica F. Serum ionized magnesium levels in type 2 diabetic patients with microalbuminuria or clinical proteinuria. Am J Nephrol. 2000 May-Jun;20(3):187-92.
7. Prabodh S, Prakash DS, Sudhakar G, Chowdary NV, Desai V, Shekhar R. Status of copper and magnesium levels in diabetic nephropathy cases: a case-control study from South India. Biol Trace Elem Res. 2011 Jul;142(1):29-35.
8. Ganesh, V., Murugan, M., Goud, V. G., & Gangannagari, V. K. (2022). Correlation of urinary nephrin with albubinuria to predict early onset of nephropathy in patients with type 2 diabetes mellitus. International Journal of Health Sciences, (III), 4621-4630.
9. Veluri, G., Murugan, M., Palem, S. P., Gangannagari, V. K. (2022). Serum Adiponectin as a Diagnostic Marker of Nephropathy among Patients with Type 2 Diabetes Mellitus: A Cross-sectional Study. Journal of Clinical & Diagnostic Research, 16(11).
10. Veluri G, Mannangatti M. Urinary Nephrin is a Sensitive Marker to Predict Early Onset of Nephropathy in Type 2 Diabetes Mellitus. J Lab Physicians. 2022 Oct 26;14(4):497-504.
11. Feng J, Wang H, Jing Z, Wang Y, Wang W, Jiang Y, et all. Relationships of the Trace Elements Zinc and Magnesium With Diabetic Nephropathy-Associated Renal Functional Damage in Patients With Type 2 Diabetes Mellitus. Front Med (Lausanne). 2021 Mar 30;8:626909.
12. Sakaguchi Y, Shoji T, Hayashi T, Suzuki A, Shimizu M, Mitsumoto K, et all. Hypomagnesemia in type 2 diabetic nephropathy: a novel predictor of end-stage renal disease. Diabetes Care. 2012 Jul;35(7):1591-7.
13. Halawa N, Elsaid TW, El Wakeel LM, Shawki MA. Impact of magnesium supplementation on clinical outcome and disease progression of patients with diabetic nephropathy: a prospective randomized trial. Ther Adv Chronic Dis. 2023 Dec 12;14:20406223231214641.
14. Zaid MH, Al-Fartusie FS, Pazhang Y, Kader S. Evaluation of lipid profile, liver function enzymes, and trace elements in Iraqi diabetic nephropathy patients. Biometals. 2024 Dec;37(6):1565-1574.
15. Joy SS, George TP, Siddiqui K. Low magnesium level as an indicator of poor glycemic control in type 2 diabetic patients with complications. Diabetes Metab Syndr. 2019 Mar-Apr;13(2):1303-1307.
16. Zhang Y, Li Q, Xin Y, Lv W, Ge C. Association between serum magnesium and common complications of diabetes mellitus. Technol Health Care. 2018;26(S1):379-387.
17. Bherwani S, Jibhkate SB, Saumya AS, Patel SK, Singh R, Ghotekar LH. Hypomagnesaemia: a modifiable risk factor of diabetic nephropathy. Horm Mol Biol Clin Investig. 2017 Mar 1;29(3):79-84.
18. Futrakul N, Futrakul P. Biomarker for early renal microvascular and diabetic kidney diseases. Ren Fail. 2017 Nov;39(1):505-511.
19. Ganesh V, M M, Palem SP. Adiponectin Can Be an Early Predictable Marker for Type 2 Diabetes Mellitus and Nephropathy. Cureus. 2022 Jul 26;14(7):e27308.

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www.jchr.org
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20. Sales CH, Pedrosa LF, Lima JG, Lemos TM, Colli C. Influence of magnesium status and magnesium intake on the blood glucose control in patients with type 2 diabetes. Clin Nutr. 2011 Jun;30(3):359-64.
21. Rizk DV, Silva AL, Pergola PE, Toto R, Warnock DG, Chin MP, et all. Effects of Bardoxolone Methyl on Magnesium in Patients with Type 2 Diabetes Mellitus and Chronic Kidney Disease. Cardiorenal Med. 2019;9(5):316-325.
22. Masoud M, Katayoun S, Nazafarin N, Melika Z, Golshid N, Negin E. The Association Between Serum Magnesium Level and Microalbuminuria in Type 2 Diabetes Mellitus Patients. Nephro-Urol Mon. 2021 February; 13(1):e112373.
23. Nasreen T, Ferdousi S, Alam K, Sultana T, Dipta TF, Selim S. Association of serum magnesium level with microalbumin in urine of newly detected type-2 diabetes mellitus. 2018 Northern International Medical College Journal 9(2):291.
24. Rahul Kumar S, Barsha , Surendra K. A Study on Association of Serum Magnesium, Serum Uric Acid Levels and Microalbuminuria in Patients with Type 2 Diabetes Mellitus. International Journal of Current Pharmaceutical Review and Research 2025; 17(3); 1638-1643.
25. Xu B, Sun J, Deng X, Huang X, Sun W, Xu Y, et all. Low serum magnesium level is associated with microalbuminuria in chinese diabetic patients. Int J Endocrinol. 2013;2013:580685.
26. Daya RP, Dipendra K, Manoj S, Naval KY, Ramchandra K, Ravindra MS, et all. Association of serum magnesium level with poor glycemic control and renal functions in Nepalese patients with type 2 diabetes mellitus. Diabetes & Metabolic Syndrome: Clinical Research & Reviews Volume 11, Supplement 1, November 2017, Pages S417-S423.
27. Dehdashti SH, Zakerkish M, Jenabi A, Hanafi M G, Rahim F. Association of Microalbuminuria and Estimated Glomerular Filtration Rate With Carotid Intima-Media Thickness in Patients With Type 2 Diabetes Mellitus.Jentashapir J Cell Mol Biol.2015;6(2):e27584.
28. Wahid A, Verma GC, Meena CP, Pathan AR. Study of serum magnesium level in patients with type 2 diabetes mellitus and it's correlation with glycosylated hemoglobin and diabetic complications. International Journal of Advances in Medicine 2017; 4(2): 311–316.

Table 1: Criteria of the study

Inclusion criteria	Exclusion criteria
Cases: The T2DM patients diagnosed as per American Diabetic Association criteria (14) and nephropathy was diagnosed according to Kidney Disease Improvement Global Outcomes (KDIGO) criteria (15). • ACR: <30 mg/g creatinine considered as Normoalbuminuria. 30-300 mg/g creatinine considered as microalbuminuria and >300 mg/g creatinine considered as microalbuminuria. **Controls:** The healthy individuals without any illness.	The participants has history of smoking, alcoholism, women with pregnant and lactation, other types of diabetes mellitus, liver, thyroid, pancreatic, cardiovascular other types of kidney diseases, malnutrition, were excluded from this study.

Table 2: Baseline characteristics of study variables between controls and T2DM patients

Parameter	Controls			T2DM patients			P-Value
	Mean	±	SD	Mean	±	SD	
Age	42.53	±	5.13	46.61	±	7.76	0.001**
BMI	20.70	±	1.55	30.38	±	6.83	0.001**
FBS	81.83	±	7.97	164.56	±	26.84	0.001**

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HbA1c	5.01	±	0.41	8.77	±	2.16	0.001**
Serum Urea	28.95	±	6.74	95.79	±	56.87	0.001**
Serum Creatinine	0.91	±	0.17	3.01	±	1.96	0.001**
Insulin	9.76	±	1.78	18.47	±	8.90	0.001**
eGFR	89.15	±	6.55	40.51	±	33.59	0.001**
ACR	18.10	±	4.01	346.66	±	337.29	0.001**
Serum magnesium	1.93	±	0.26	0.76	±	0.27	0.001**

Table 3: comparison of study variables between the study subjects

Parameters	Controls			T2DM with Normoalbuminuria			T2DM with Microalbuminuria			T2DM with Macroalbuminuria			P-value
	Mean	±	SD	Mean	±	SD	Mean	±	SD	Mean	±	SD	0.001**
Age	42.53	±	5.13	40.83	±	3.43	48.65	±	3.15	56.35	±	5.05	0.001**
BMI	20.70	±	1.55	22.18	±	1.60	31.94	±	3.15	37.02	±	3.63	0.001**
FBS	81.83	±	7.97	141.50	±	7.99	159.30	±	12.30	192.88	±	24.23	0.0001**
HbA1c	5.01	±	0.41	6.87	±	0.47	8.31	±	0.95	11.09	±	1.91	0.0001**
Serum Urea	28.95	±	6.74	30.35	±	8.57	94.65	±	17.85	162.38	±	23.11	0.0001**
Serum Creatinine	0.91	±	0.17	1.01	±	0.28	2.68	±	0.45	5.34	±	1.30	0.0001**
Insulin	9.76	±	1.78	12.13	±	2.55	21.15	±	1.85	30.86	±	5.11	0.0001**
eGFR	89.15	±	6.55	86.75	±	7.49	22.54	±	5.33	12.24	±	3.68	0.0001**
ACR	18.10	±	4.01	16.96	±	4.39	226.53	±	35.66	796.52	±	109.52	0.0001**

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Serum Magnesium	1.93	±	0.26	0.89	±	0.27	0.81	±	0.26	0.60	±	0.17	0.0001**

Table 4: Correlation of serum magnesium with biochemical and clinical parameters of the study

Parameter	r	P
Age	-0.38	0.001**
BMI	-0.64	0.001**
FBS	-0.82	0.001**
HbA1c	-0.68	0.001**
Urea	-0.60	0.001**
Creatinine	-0.57	0.001**
Insulin	-0.62	0.001**
eGFR	0.62	0.001**
ACR	-0.55	0.001**

Table 5: The Receivers operating characteristics between urinary ACR, eGFR and serum magnesium

Parameters	AUC	95% CI For Value	Cut Off Value	Sensitivity	Specificity	P Value
Urinary ACR (mg/g creatinine)	0.573	0.458 to 0.683	0.2750	32.50	95.00	0.2623
eGFR (ml/min)	0.565	0.450 to 0.676	0.1750	47.50	70.00	0.3152
Serum magn	0.989	0.935 to	0.9500	95.00	100.00	0.0001
esium		1.000				

Figure 1: Shows the study participants'

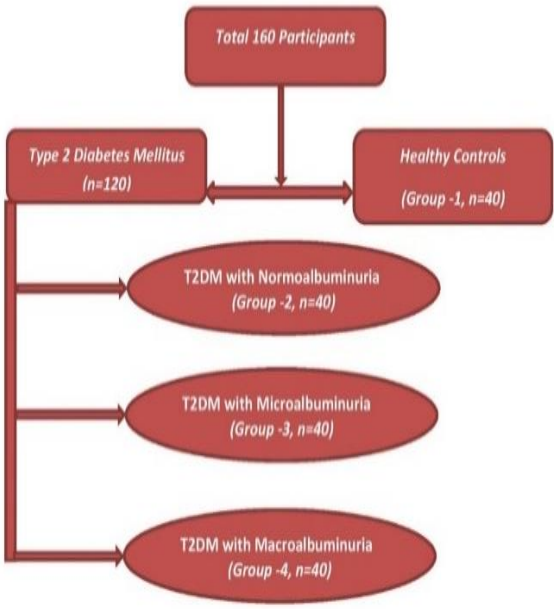

Figure 2 shows the comparison of eGFR, urinary ACR and Serum Magnesium in between study subjects

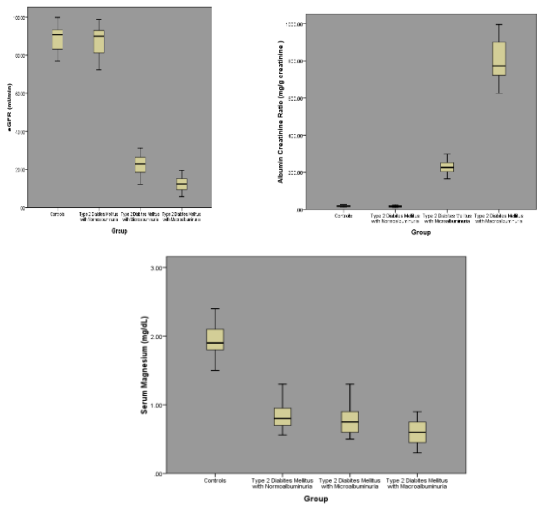

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Figure 3: Scatterplots between serum magnesium and FBS, HbA1c, Insulin, eGFR and urinary ACR