



The Role of Serum Magnesium for Early Detection of Nephropathy in Patients with Type 2 Diabetes Mellitus

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KEYWORDS

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y and Type
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ABSTRACT:

Introduction: Magnesium is an essential mineral have insulin sensitivity and antioxidant properties. The decreased levels of magnesium cause type 2 diabetes mellitus and related kidney problems

Objectives: This study aimed to evaluate the role of magnesium for early prediction of kidney damage in different stages of type 2 diabetic nephropathy and controls.

Methods: Thirty (30) type 2 diabetes mellitus with normo, 30 micro, 30 macro albuminuria patients and 30 control subjects were recruited in this study. The basic parameters FBS, Lipid profile, HbA1c, urea, creatinine, urinary albumin creatinine, eGFR levels were measured by commercially available kits for all the study subjects. Additionally, the serum magnesium, levels also measured by calmagite indicator method in all the study subjects.

Results: The serum magnesium levels significantly and drastically decreased in type 2 diabetes mellitus with normo, micro and macro albuminuria when compared to controls. The serum magnesium significant negatively correlated with blood sugars, glycated haemoglobin, urinary albumin creatinine ratio and positively correlated with eGFR. The ROC curve analysis shown the magnesium has highest sensitivity and specificity than urinary albumin creatinine ratio and eGFR.

Conclusions: The serum magnesium levels are reversibly decreased in all the groups of type 2 diabetes mellitus patients. We suggest determining serum magnesium might be used as an early detectible and prognostic marker for nephropathy in patients with type 2 diabetes mellitus.

1. Introduction

Type 2 diabetes mellitus is a chronic metabolic illness due to hyperglycemia. Both environmental and genetic variables contribute equally to the development of this prevalent metabolic disease (1-2). According to projections, 415 million diabetic people across the worldwide in 2015 and it is expected up to 650 million by 2030. India has the greatest percentage of diabetes cases worldwide, earning it the moniker, diabetes capital of the world around 65 million by 2013 and it is also expected to reach around 103 million by 2030 (3-4). The majority of patients have hyperglycemia symptoms at first, which, if persistent, can result in long-term issues that eventually malfunction the heart, kidneys, nerves, eyes, and blood vessels (5-6).

Nephropathy is a most common micro vascular complication in patients with type 2 diabetes mellitus. The nephropathy predicted to go through distinct stages such as glomerular hyper filtration, microalbuminuria, and overt proteinuria (7). The microalbuminuria is currently using gold standard method for detecting nephropathy. But the recent studies are reported that the micro albumin is not a sensitive and specific marker for nephropathy because it has lot of flows i.e many micro albuminuria patients convert into normo albuminuria state, the normo albuminuria patients shown an advanced renal pathophysiology, and also it is elevated in other disease conditions (8-10).

Magnesium is a principal element and involves improving insulin sensitivity, lowering oxidative stress,



and reduces the systemic inflammation. The recent research studies are reported the type 2 diabetes mellitus patients have been found to have a higher prevalence of magnesium insufficiency and poor control of blood sugar (11-12). The previous studies shown hypomagnesemia has been associated with impaired glucose regulation as well as an increased risk of retinopathy, neuropathy, nephropathy, and macrovascular consequences (13-14).

2. Objectives

The present study focused the serum magnesium role in type 2 diabetes mellitus and either this can be used early predictable marker in place of micro albumin for diagnosis and prognosis of nephropathy.

3. Methods

The current case control study included 90 type 2 diabetes mellitus patients diagnosed as per american diabetic association criteria (15). This study conducted at Raichur Institute of Medical Sciences, Raichur, Karnataka. The type 2 diabetes mellitus patients further divided into two groups based on their albumin creatinine ratio and also, we included 30 age and gender matched healthy individuals consider as controls shown in Table 1. The study conducted after obtaining approval from the institutional ethics committee and obtained informed consent form from all the study subjects.

Inclusion & Exclusion criteria

All the study subjects age around 30-70 years. The type 2 diabetes mellitus patients diagnosed as per the american diabetes association criteria. The micro albumin levels <30 mg/g creatinine is considered as T2DM with Normo albuminuria, The micro albumin levels 30-299 mg/g creatinine is considered as T2DM with Micro albuminuria and The micro albumin levels >300 mg/g creatinine is considered as T2DM with Macro albuminuria according to kidney disease improvement global outcomes criteria (16). The controls don't have any illness are included. The women with pregnant and lactating, the subjects has h/o smoking, alcoholism, other types of diabetes mellitus, thyroid, liver, cardiac, other types of kidney diseases. The subjects not willing to participate excluded from the study.

Collection of samples

Five (5) millilitres of overnight fasting blood sample collected from all the study participants, later 1mL transferred to grey colour anticoagulant tube, 1mL

transferred to purple colour anticoagulant tube and remaining 3mL transferred to red colour tube. Additionally, we also collected fasting spot urine sample. All the samples were separated by the process of centrifugation. The separated samples transferred to properly labelled aliquots and stored at -50^oc until biochemical analysis was be done.

Methods and Instrumentation

The fasting blood sugar and lipid profile was determined by glucose oxidase peroxidase method, cholesterol oxidase peroxidase method, enzymatic method, selective inhibitory method and VLDL and LDL calculated by Friedewald's formula. The HbA1c analysed by immunoturbidometry method. The magnesium was measured by calmigate indicator method. The albumin/creatinine ratio was calculated by urinary albumin/creatinine ratio. The estimated glomerular filtration rate was calculated by modified diet in renal diseases.

Statistical Analysis

The distribution of data was done by kolmogorov smirnov test and data was represented as mean \pm standard deviation. The analysis of variance done for comparison of variables between the groups and the pearson's correlation done between the variables. The receivers operating character curve analysis was done to identify sensitive and specific marker for early detection of nephropathy in between the type 2 diabetes with normo albuminuria and controls. The statistical analysis done by using microsoft excel spread sheets and statistical package for social version 20.0. A probability value <0.05 consider as statistically significant.

4. Results

5. The table 2 shows the comparison of study variables between the controls and type 2 diabetes mellitus patients. The age shown significant between controls and type 2 diabetes mellitus patients (P=0.001**). The BMI, FBS, HbA1c, TC, TGL, VLDL and LDL significantly elevated in type 2 diabetes mellitus patients when compared to controls (P=0.001**). The albumin creatinine ratio highly and significantly enhanced in in type 2 diabetes mellitus patients when compared to controls (P=0.001**). The HDL, eGFR, and magnesium drastically decreased in type 2 diabetes



mellitus patients when compared to controls (P=0.001**).

The table 3 shows the comparison of study variables between the controls and three groups of type 2 diabetes mellitus patients. The age shown significant between controls and three groups of type 2 diabetes mellitus patients (P=0.001**). The BMI, FBS, HbA1c, TC, TGL, VLDL and LDL significant and drastically elevated in type 2 diabetes mellitus patients with normo, micro, and macro albuminuria when compared to controls (P=0.001**). The type 2 diabetes mellitus patients with macro, micro albuminuria shown very high significant levels of albumin creatinine ratio when compared to type 2 diabetes mellitus patients with normo albuminuria and controls (P=0.001**). The HDL, eGFR, and magnesium significant and drastically reduced in type 2 diabetes mellitus patients with macro, micro, and normo albuminuria when compared to controls (P=0.001**).

The table 4 illustrates the pearson's correlation analysis between serum magnesium and other study variables. The serum magnesium was significant and negatively correlated with BMI, FBS, TC, TGL, VLDL, LDL, HbA1c, and urinary albumin creatinine ratio respectively P value is 0.001**. There was a significant positive correlation between serum magnesium and eGFR, and HDL (P=0.001**).

The table 5 illustrates the receiver operating characteristic curve analysis for sensitive and specific marker for nephropathy in type 2 diabetes mellitus patients with normo albuminuria and controls. The urinary ACR and eGFR not sensitive, specific markers for nephropathy due to its not shown in a significance at AUC (0.562 and 0.548, P=0.344 and 0.471). The serum magnesium shown very high significant at AUC, high sensitivity and specificity (100) respectively P value is <0.0001**. The type 2 diabetes mellitus with macro, micro albuminuria patients shown drastically decreased levels of eGFR, when compared to type 2 diabetes mellitus with normo albuminuria and controls (figure 1).

The type 2 diabetes mellitus with macro, micro albuminuria patients shown increased levels of BMI,

when compared to type 2 diabetes mellitus with normo albuminuria and controls (figure 2).

The type 2 diabetes mellitus with macro, micro, and normo albuminuria patients shown elevated levels of HbA1c, when compared to controls (figure 3).

The type 2 diabetes mellitus with macro, micro, albuminuria patients shown elevated levels of albumin creatinine ratio, when compared to type 2 diabetes mellitus with normo albuminuria and controls (figure 4).

The type 2 diabetes mellitus with macro, micro and normo albuminuria patients shown drastically decreased levels of eGFR, when compared to controls (figure 5).

The serum magnesium shown highest significance at AUC and very high sensitive and specific when compared to eGFR and urinary ACR (P=0.0001**) (figure 6).

6. Discussion

According to numerous researches, metabolic disturbances and electrolyte abnormalities may result in long-term consequences of type 2 diabetes mellitus. Additionally, earlier research reported magnesium deficiency is a significant factor in the development of type 2 diabetes mellitus and nephropathy (17-19). As a result, assessing the serum magnesium level may help prevent and treat many type 2 diabetes mellitus problems.

The current study's assessment of serum magnesium status in patients with type 2 diabetes revealed a marked drop in instances as compared to controls and particularly the type 2 diabetes mellitus with macro, micro albuminuria patients compared to normo albuminuria. Similarly, another previous studies also observed the diabetes mellitus with overt proteinuria or microalbuminuria had significantly lower serum magnesium levels than the Normoalbuminuria group (20-21). In type 2 diabetes mellitus patients with magnesium deficiency, intracellular calcium build up occurs because magnesium is a modest, natural calcium antagonist (22). The development of insulin resistance may result from this elevated intracellular calcium changing how sensitive the cells are to insulin. Therefore, a potential mechanism linking serum



magnesium to microalbuminuria could be an increase of insulin inhibition (23-24). The recent study reported that in type 2 diabetes patients with insulin resistance or insufficiency, poor tubular absorption of magnesium can also result in hypomagnesemia. Insulin resistance and hypomagnesemia can thereby raise the risk of microalbuminuria (25). Another study also discovered a high correlation between oxidative stress and hypomagnesemia. A magnesium deficiency may result in specific alterations in endothelial cells that lead to oxidative stress and inflammation-induced endothelial cell damage (26).

We discovered a negative correlation between urine micro albumin, and serum magnesium levels and positive correlation between eGFR and serum magnesium. Additionally, the ROC curve analysis revealed the serum magnesium shown highest sensitivity and specificity then urinary ACR and eGFR. The serum magnesium can served as early detection of nephropathy in patients with diabetes mellitus.

Conclusion:

Based on these study findings, we suggest the serum magnesium might be used as early detectable and prognostic marker for nephropathy in patient with type 2 diabetes mellitus.

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Table 1: Study groups and no of study subjects for each group.

Group	Name of the subjects	No. of subjects
Group-1	Controls	30
Group-2	Type 2 Diabetes Mellitus with Normo albuminuria	30
Group-3	Type 2 Diabetes Mellitus with Micro albuminuria	30
Group-4	Type 2 Diabetes Mellitus with Macro albuminuria	30

Table 2: Shows the comparison of study variables between the controls and type 2 diabetes mellitus patients.

Parameters	Controls			Type 2 Diabetes Mellitus			P-Value
	Mean	±	SD	Mean	±	SD	
Age (Yes)	44.2	±	6.3	49.1	±	7.28	0.001**
BMI (kg/m ²)	22.0	±	1.5	31.5	±	6.21	0.001**
FBS (mg/dL)	83.9	±	8.2	159.	±	28.1	0.001**
eGFR (ml/min)	91.3	±	7.5	41.1	±	35.8	0.001**
Total Choleste	160.	±	15.	249.	±	63.4	0.001**
	43		06	68		0	



Triglycerides (mg/dL)	-0.70	0.001**
HDL (mg/dl)	0.72	0.001**
VLDL (mg/dl)	-0.67	0.001**
LDL (mg/dl)	-0.68	0.001**
HbA1c (%)	-0.71	0.001**
Albumin Creatinine Ratio (mg/g creatinine)	-0.60	0.001**

Table 5: Receiver operating characteristic curve analysis for sensitive and specific marker for nephropathy.

Parameter	AUC	95% CI for Value	Cutoff Value	Sensitivity	Specificity	P Value
Urinary ACR (mg/g creatinine)	0.562	0.447 to 0.673	0.200	97.50	22.50	0.344
eGFR (ml/min)	0.548	0.433 to 0.660	0.275	90.00	37.50	0.471
Serum magnesium (mg/dL)	1.000	0.955 to 1.000	1.000	100.00	100.00	<0.001

Figure 2: Comparison of BMI in between study groups.

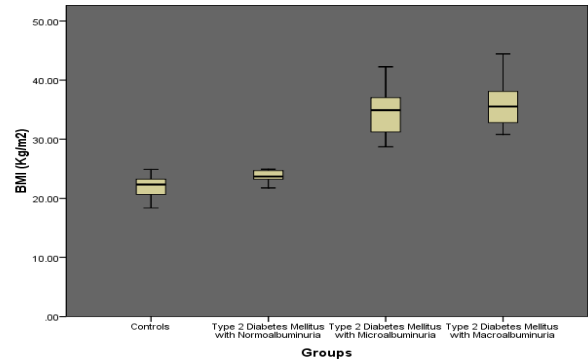


Figure 3: Comparison of HbA1c in between study groups.

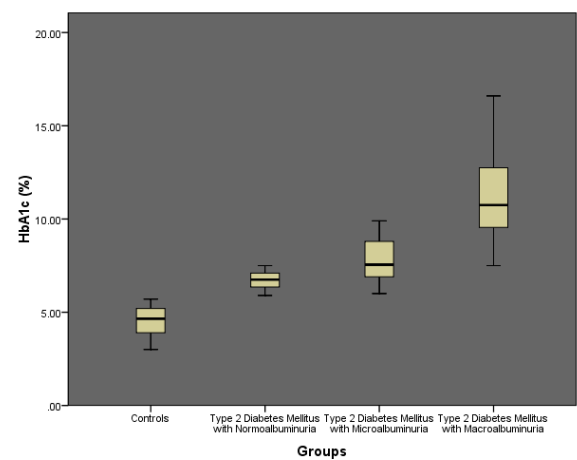


Figure 4: Comparison of albumin creatinine ratio in between study groups.

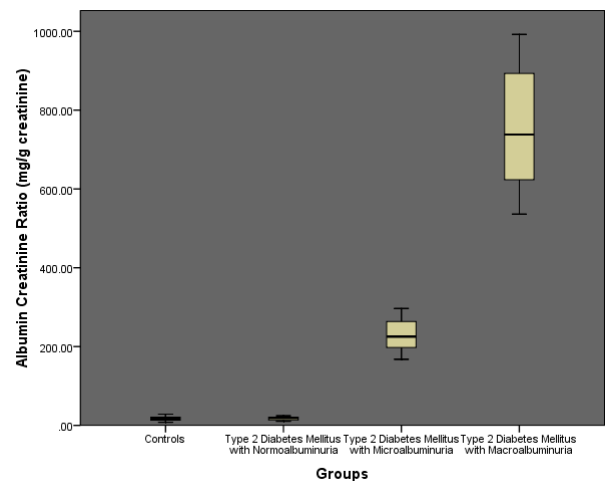


Figure 1: Comparison of eGFR in between study groups

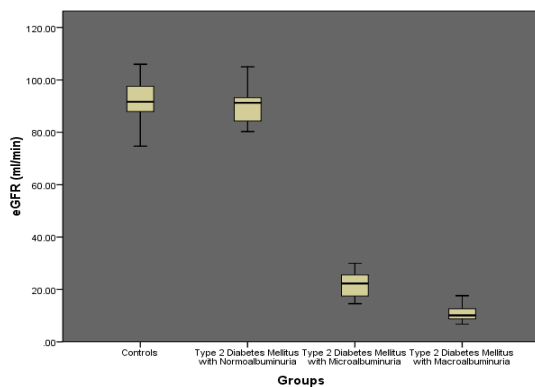




Figure 5: Comparison of serum magnesium ratio in between study groups

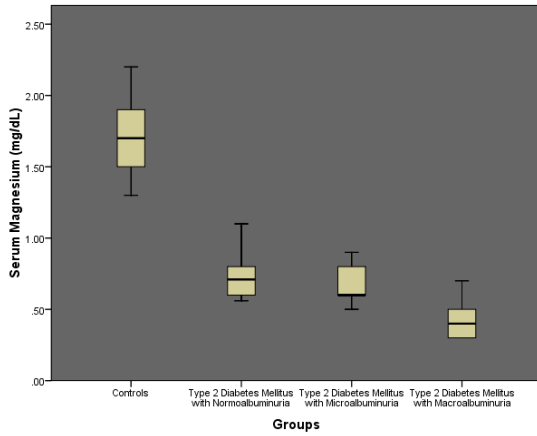


Figure 6: ROC Curve analysis between serum magnesium and eGFR, urinary ACR.

