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Original Research Article

A study on association of serum magnesium, serum uric acid levels and microalbuminuria in patients with type 2 diabetes mellitus

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ABSTRACT

Background: Microalbuminuria is multifactorial and it is an important marker for diabetic nephropathy. The aim of the study was to assess the incidence and association of serum magnesium levels, serum uric acid levels and microalbuminuria in patients with type 2 DM.
Methods: This study was a cross-sectional study conducted for a period of 2 years from October 2015 to September 2017, where the patients diagnosed as type 2 DM admitted in AJIMS were taken up for the study. All the patients' blood sample was sent for estimation of serum magnesium, serum uric acid, FBS, PPBS, HBA_1C and urine spot albumin:creatinine ratio.
Results: In our study, out of 100 patients with type 2 diabetes, 79 patients had microalbuminuria. Out of these, 83.3% (N=75) was having hypomagnesemia ($p<0.000$) associated with microalbuminuria. Hyperuricemia was seen in 63% (N=63) of the population but 79.4% (N=50) hyperuricemics were associated with microalbuminuria($p<0.000$).
Conclusions: There was a significant microalbuminuria in patients with type 2 DM, with reduced serum Mg levels and elevated serum uric acid levels as compared with patients who had serum Mg and uric acid levels within the normal range.

Keywords: Magnesium, Uric acid, Microalbuminuria, Type 2 diabetes

INTRODUCTION

Diabetes mellitus has complications like cardiovascular, renal and different types of microangiopathies have been well documented. As per the recent reports by the international federation of diabetes, globally 415 million adults are suffering from diabetes, and also estimated that the numbers are likely to reach around 642 million by 2045.[1]

Magnesium is considered being one of the most important minerals for human body as it plays important role in the phosphorylation reactions of glucose and its metabolism.[2] Its lower intake and low serum level are linked to with insulin resistance, and type-2 diabetes mellitus (T2DM).[3] It's also observed that low Mg level was associated with complications of diabetes like diabetic retinopathy in caucasians but not in black African diabetics.[4]

Urate (soluble form of uric acid) is known to scavenge superoxide radicals, hydroxyl radicals and other free radicals and may have therapeutic influences.[5] In spite of this, definitive role of uric acid in diabetes is not yet understood. but hyperuricemia in glucose intolerance and uncontrolled diabetes is thought to be closely associated.[6,7] Therefore, this study aims to study the association between serum Mg level, uric acid and

incidence of microalbuminuria in type 2 diabetes mellitus.

METHODS

The present study was a hospital based, cross-sectional study, conducted for a period of two years from October 2015 to September 2017, carried out on 100 patients diagnosed with type 2 diabetes mellitus and admitted to AJ institute of medical sciences & research centre (AJIMS), Mangaluru. The study was done in the department of general medicine AJIMS, Mangaluru who satisfied the inclusion criteria, after taking an informed written consent from all the subjects.

Inclusion and exclusion criteria

All the type 2 diabetic patients hospitalized at AJ institute of medical sciences & research centre, Mangaluru of any age and gender are included in the study. Those Patients with type 1 diabetes mellitus, patient with history of alcohol intake, gout fever, UTI (urinary tract infections), arthritis, acute myocardial infarction, recent major surgery/major trauma, hypertensive, recent (6 months) intervention with ACE inhibitors/ARB and those on chemotherapeutic agents (anti-neoplastic drugs) were excluded from the study.

A pre-structured proforma was used to collect the data. Detailed history was taken from the patients about the fever, chest pain, breathlessness, lifestyle, history of chronic disease, current medications including anti diabetic drugs (oral agents or Insulin), anti-hypertensive agents, uricosuric drugs and chemotherapeutic agents. Personal history (alcohol etc.) was taken. Fasting and post prandial sugar levels, HBA1C levels for diagnosis of type 2 DM, serum magnesium and serum uric acid levels were also estimated. Urinary albumin excretion was assessed by urinary albumin: creatinine ratio in spot sample. Those who die during the hospital stay, date & cause of death was recorded. The patients were divided into the following groups according to the degree of albuminuria as follows: normal: <30 mg/day, microalbuminuria: 30-300 mg/day and macroalbuminuria: >300 mg/day.[8] The serum uric acid normal range is 3-7 mg/dl in male whereas it's 2.5-6 mg/dl in female.[9] For serum magnesium, a serum level of 1.4.-2 mg/dl is considered to be in normal range.[10]

Statistical analysis

Collected data from the study population were entered into Microsoft Excel 2007 and Epi Info 7. Their demographic data analysis was performed. Descriptive data were expressed as frequency, percentage, Chi-square test, Fisher Exact and 't' test were applied whenever applicable.

The entire data were analysed using the software graph pad, $p<0.05$ was considered to be statistically significant and $p<0.001$ was considered to be statistically highly significant.

RESULTS

This study was a cross-sectional study conducted for a period of 2 years from October 2015 to September 2017, where 100 patients diagnosed as type 2 DM admitted in AJIMS were taken up for the study. These were our observations.

Table 1: Age distribution in the study group.

Age groups (years)	N	%
31-40	18	18
41-50	16	16
51-60	39	39
61-70	19	19
Above 70	8	8
Total	100	100

Demographic data

In our study, 66% of the population was above the age of 50 years. Maximum being in the age group of 51-60 years.

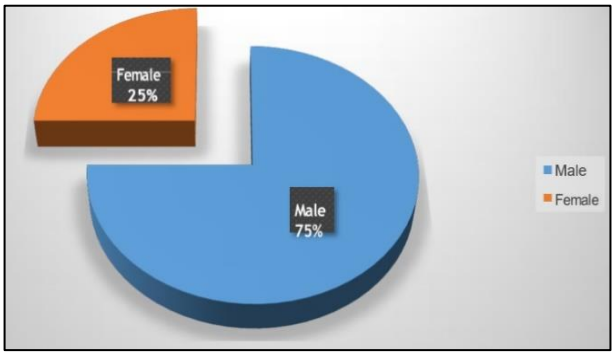

Figure 1: Gender distribution in the study group.

In our study most patients were male comprising 75% of the study population. The male to female ratio was 3:1.

Laboratory data

Microalbuminuria: In our study, 79 out of 100 patients had a positive microalbuminuria and 14% showed macroalbuminuria. Serum magnesium levels were on the lower side in 90% of the population and only 10% had levels within the normal range in our study. High levels of serum Mg were not seen in our study.

There was a significant reduction in serum Mg levels in patients with T2DM. The exact cause of hypomagnesemia in diabetes mellitus in not known. Poor dietary intake, impaired absorption of magnesium, increased urinary loss due to hyperglycemia and osmotic diuresis may be the contributory factors. Magnesium depletion is also said to increase the risk of secondary

complications. In our study, there was a strong positive correlation between, hypomagnesemia and microalbuminuria, with highly significant p value of 0.000. Out 79 study population with microalbuminuria, 74 patients had low serum Mg levels, i.e., 95%.

Table 2: Microalbuminuria in the study group.

Albuminuria	N	%
Microalbuminuria	79	79
Macroalbuminuria	14	14
Normal	7	7
Total	100	100

Table 3: Serum magnesium levels in the study group.

Serum magnesium	N	%
Low	90	90
Normal/elevated	10	10
Total	100	100

Serum uric acid: Serum uric acid levels were elevated in 63% of the study population whereas 37% were within the normal range or low.

In our study there was an inverse association between serum uric acid levels and T2DM, as seen in above table and graph. The exact cause of hyperuricemia in T2DM is not clearly understood but could be associated with oxidative stress and production of tumor necrosis factor alpha (TNF-α), which are both related to the development of DM. Uric acid also decreases endothelial nitric oxide production and leads to endothelial dysfunction and insulin resistance.

In our study, there was a positive correlation between, high uric acid levels and microalbuminuria with a highly significant value of 0.000. Out of 79 study population with microalbuminuria, 50 (63%) had elevated serum uric acid levels.

Table 4: Serum magnesium and microalbuminuria.

Serum magnesium	Microalbuminuria; N (%)			Total N (%)
	Microalbuminuria	**Macroalbuminuria**	**Normal**	
Low	75 (83.3)	14 (15.6)	1 (1.1)	90 (100)
Normal/elevated	4 (40.0)	0 (0)	6 (60.0)	10 (100)
Total	79 (79.0)	14 (14.0)	7 (7.0)	100 (100)

p=0.00, number of valid cases=79.

Table 5: Serum uric acid levels in the study group.

Serum uric acid	N	%
Elevated	63	63
Normal/low	37	37
Total	100	100

Table 6: Serum uric acid and microalbuminuria.

Serum uric acid	Albuminuria; N (%)			Total N (%)
	Microalbuminuria	**Macroalbuminuria**	**Normal**	
Elevated	50 (79.4)	13 (20.6)	0 (0)	63 (100)
Normal/low	29 (78.4)	1 (2.7)	7 (18.9)	37 (100)
Total	79 (79.0)	14 (14.0)	7 (7.0)	100 (100)

p=0.00, number of valid cases=79.

DISCUSSION

In patients with type 2 diabetes, microalbuminuria is associated with a twofold to fourfold increase in the risk of death. Microalbuminuria being a well-known early predictor of diabetic nephropathy and is due to increased vascular permeability as well as endothelial damage. In our study, 66% of the study population was above 50 years of age, as in study by Tseng et al where the mean age of T2DM was 62.8±10.8 years, and in a study by Xu et al the mean age was 61.11±10.01 years.[11,12]

In this study, the mean duration of diabetes mellitus in diabetic patients with microalbuminuria was 9.70±4.66 years and in diabetic patients with normoalbuminuria was 3.56±2.31 years.

The duration of diabetes mellitus was significantly higher in diabetic patients with microalbuminuria when compared to diabetic patients with normal albuminuria in our study. In the present study, 95% of the patients with microalbuminuria showed hypomagnesemia. There was a statistically significant increased incidence of

microalbuminuria in patients with hypomagnesemia as compared with normal levels.

Our findings were similar to study done by Xu et al who showed that serum magnesium was inversely associated with the prevalence of microalbuminuria.[13] Gupta et al also showed increased incidence of microalbuminuria in T2DM patients with hypomagnesemia.[14] The exact relationship between hypomagnesemia and microalbuminuria in DM is not known. Oxidative stress is becoming increasingly recognized as an important factor for microalbuminuria.[15] Magnesium has been reported to possess antioxidant property.

Hence, oxidative stress may be one of the mechanisms that underlie the association between serum Mg and microalbuminuria. Magnesium depletion is said to reduce the insulin sensitivity, thereby increasing the risk of secondary complications.[16] In our study, 63% of the population with positive microalbuminuria showed hyperuricemia. There was statistically significant increased incidence of microalbuminuria in patients with hyperuricemia as compared with normal/low serum uric acid levels.

The present study shows a strong relationship between hyperuricemia and microalbuminuria, which was similar to findings of study done by Chin-Hsiao. Our findings were similar to study done by Bonakdaran et al which also concluded that higher serum uric acid concentrations were associated with a greater probability of albuminuria in patients with type 2 diabetes mellitus.[17] Uric acid is the final breakdown product of adenosine, which plays an important role in the pathophysiology of insulin resistance.[18] Hyperinsulinemia resulting from insulin resistance can decrease the renal excretion, increase the renal absorption, and increase the production of uric acid. Microalbuminuria is an integral part of metabolic syndrome characterized by insulin resistance.[19] Hence it is important to monitor serum magnesium and serum uric acid levels in type 2 diabetic patients to prevent the onset and progression of diabetic nephropathy.

Limitations

The study was a hospital-based study with relatively small sample size; therefore, it may not represent the scenario of different parts of the country.

CONCLUSION

Based on the results of present study, serum magnesium level was inversely related with the incidence of microalbuminuria whereas there was linear association with high serum uric acid level. Good glycemic control and correction of hypomagnesemia and hyperuricemia could be effective to reduce the incidence of microalbuminuria and progression of renal impairment in type 2 diabetic mellitus.

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