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Original Research Article

Relationship of Serum Magnesium, Serum Uric Acid Levels and Microalbuminuria in Patients with Type 2 Diabetes Mellitus

Reena Singh[1], Ronak Kapadia[2], Paras Shah[3], Girish Narsinghani[4]

[1]Assistant Professor, Department of Medicine, GCS Medical College and Research Center Ahmedabad, Gujarat, India

[2]Assistant Professor, Department of Medicine, GCS Medical College and Research Center Ahmedabad, Gujarat, India

[3]Assistant Professor, Department of Medicine, GCS Medical College and Research Center Ahmedabad, Gujarat, India

[4]Assistant Professor, Department of Medicine, GCS Medical College and Research Center Ahmedabad, Gujarat, India

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Corresponding author: Dr Girish Narsinghani

Conflict of interest: Nil

Abstract

Background: Diabetic nephropathy is a serious side effect of diabetes mellitus. Microalbuminuria is a sign of diabetic nephropathy in people with type II mellitus. Studies have demonstrated that treatments to tightly regulate blood sugar and blood pressure can reverse the development of microalbuminuria. Microalbuminuria is multifactorial and it is an important marker for diabetic nephropathy.

Aim and Objectives: Present study aims to study the relationship between serum Mg level, uric acid and incidence of microalbuminuria in type 2 diabetes mellitus.

Material and Methods: The present study was a hospital based, cross-sectional study, conducted for a period of one and half years, carried out on 250 patients diagnosed with type 2 diabetes mellitus and admitted to tertiary care institute of India. All the patients' blood sample was sent for estimation of serum magnesium, serum uric acid, FBS, PPBS, HBA1C and urine spot albumin:creatinine ratio.

Results: In our study, 198 out of 250 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. Serum uric acid levels were elevated in 62.8% of the study population whereas 37.2% were within the normal range or low. There was a positive correlation between, high uric acid levels and microalbuminuria with a highly significant value of 0.001.

Conclusion: 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.

Keywords: Diabetes mellitus, Hypomagnesemia, Serum magnesium, Serum uric acid

Introduction

A chronic metabolic disorder called diabetes mellitus causes abnormal protein and lipid metabolism in addition to hyperglycemia [1]. Diabetes mellitus involves well-known consequences as cardiovascular, renal, and other types of microangiopathies. This widespread metabolic disease is caused by both genetic and environmental causes. Most patients first show signs of hyperglycemia, which if left untreated can result in long-term issues that eventually affect organs like the kidneys, heart, blood vessels, nerves, and eyes [2].

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 [3]. its lower intake and low serum level are linked to with insulin resistance, and type-2 diabetes mellitus (T2DM) [4] The percentages of free magnesium, protein-bound magnesium (mainly albumin), and complexed magnesium in the human body is roughly as follows: free magnesium, 55%; protein-bound magnesium, 30%; and complexed magnesium, 15%. More than 300 distinct enzymes involved in the metabolism of fuels (carbohydrate, proteins, lipids, and nucleic acids) are known to be activated by magnesium. Additionally, it aids in the movement of electrolytes across cell membranes [5].

The sodium and potassium electrolyte concentration gradient is maintained by the Na+/K+-ATPase, which also aids in the transportation of glucose. A hypomagnesemic state can alter or modify its activity [6]. Magnesium is also involved in the process of insulin production, binding, and action. Faulty tyrosine kinase activity on the insulin receptors, which may be brought on by hypomagnesaemia, can result in post receptor resistance to insulin as well as defective or reduced cellular utilisation of glucose. 90% of all type 2 DM cases have both insulin resistance and a gradual impairment in insulin secretion [8]. When chronic, the magnesium deficiency can cause insulin resistance and impaired glucose uptake, further reducing the already low levels of insulin sensitivity seen in type 2 DM patients [9]. Alterations in Mg status usually accompany Type 2 Diabetes Mellitus. In those with Type 2 diabetes, hypomagnesemia seems to have a deleterious impact on both glucose homeostasis and insulin sensitivity [10].

Therefore, it is clear that Mg and Type 2 Diabetes mellitus are closely related, and roughly one-third of those with Type 2 DM have hypomagnesemia, which is mostly brought on by increased renal excretion [11]. Viberti *et al*. published the first study on microalbuminuria in diabetic individuals in 1982 [12]. Numerous studies have shown that microalbuminuria, which is known to be linked to oxidative stress and changed levels of magnesium in blood, increases the risk of complications in diabetes patients. These difficulties can gradually affect the cardiovascular system, eyes, kidneys, and nerves [13].

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].

Aims and Objectives

This study aims to study the association between serum Mg level, uric acid and incidence of microalbuminuria in type 2 diabetes mellitus.

Material and Methods

The current study involved 250 individuals with type 2 diabetes mellitus who were

admitted to an Indian tertiary care facility over the course of a 1.5-year period. It was a hospital-based, cross-sectional study. The institutional ethical committee provided its ethical approval, and each subject provided signed informed permission.

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: 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

Microsoft Excel 2007 was used to compile and input the collected data, which was then exported to the data editor page of SPSS version 15 for analysis (SPSS Inc., Chicago, Illinois, USA). The level of significance and confidence level for each test were set at 5% and 95%, respectively.

Results

In our study, 66% of the population was above the age of 50 years. Maximum being in the age group of 51-60 years. In our study most patients were male comprising 74% of the study population.

In our study, 198 out of 250 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.

In patients with T2DM, serum Mg levels significantly decreased. Hypomagnesemia in diabetes mellitus has an unknown specific cause. The contributing variables may include poor food intake, reduced magnesium absorption, increased urine loss brought on by hyperglycemia, and osmotic diuresis. The likelihood of subsequent problems is also thought to rise with magnesium deficiency. In our investigation, there was a statistically significant positive connection between hypomagnesemia and microalbuminuria. ($p<0.05$) 185 of the 198 study participants who had microalbuminuria had low serum magnesium levels. Serum uric acid levels were elevated in 62.8% of the study population whereas 37.2% 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 0.001. Out of 198 study population with microalbuminuria, 125 (63.13%) had elevated serum uric acid levels.

Table 1: Age wise distribution in the study group

Age (Years)	Number	Percentage (%)
31-40	45	18
41-50	40	16
51-60	98	39.2
61-70	48	19.2
Above 70	19	7.6
Total	250	100

Table 2: Microalbuminuria in the study group

Albuminuria	Number	Percentage (%)
Microalbuminuria	198	79.2
Macroalbuminuria	35	14
Normal	17	6.8
Total	250	100

Table 3: Serum magnesium levels in the study group

Serum magnesium	Number	Percentage (%)
Low	225	90
Normal/elevated	25	10
Total	250	100

Table 4: Serum uric acid levels in the study group

Serum uric acid	Number	Percentage (%)
Elevated	157	62.8
Normal/low	93	37.2
Total	250	100

Discussion

A serious health problem for people with diabetes is diabetic nephropathy. Normal diabetic nephropathy progression was typically viewed as a downhill trend from normoalbuminuria to end-stage renal disease (ESRD) via a transitional stage marked by microalbuminuria and obvious proteinuria [14]. Diabetic nephropathy is the cause of about 30% of chronic renal failures in India [15]. Microalbuminuria (30–300 mg/day), the first clinical sign of nephropathy, is the presence of minute but elevated quantities of albumin in the urine [16]. By introducing the idea of "microalbuminuria," which is defined as an increased but clinically undetectable excretion of urine albumin, new and intriguing information has been found that has significant clinical implications for diabetes patients [17]. People with diabetes should have a yearly blood creatinine and microalbuminuria tests, according to the American Diabetes Association (ADA). Since it is possible to identify and treat the circumstances that lead to the change from normal urine excretion to microalbuminuria and from microalbuminuria to diabetic nephropathy, primary control of diabetic nephropathy is achievable [18]. The final byproduct of purine breakdown is serum uric acid [19].

Insulin resistance syndrome, a recognised risk factor for type 2 diabetes, and hyperuricemia are closely connected [20]. Although there are several potential processes linking hyperuricemia to glucose intolerance, the most important one is the link between insulin and renal resistance to urate absorption [21]. Consequently, it is important to do research on how uric acid contributes to the aetiology of type 2 diabetes.

As in studies by Tseng *et al*., where the mean age of T2DM was 62.8±10.8 years, and by Xu *et al*., where the mean age was 61.11±10.01 years, 66% of the study population in our study was over the age of 50 [22,23]. In this study, the mean time that diabetic patients with microalbuminuria experienced diabetes mellitus was 9.68±4.70 years, whereas the mean time for diabetic patients with normoalbuminuria was 3.60±2.35 years. In our study, diabetic patients with microalbuminuria had a considerably longer duration of diabetes mellitus than diabetic patients with normal albuminuria. 95% of the individuals in the current study who had microalbuminuria displayed hypomagnesemia. When compared to patients with normal levels of magnesemia, patients with hypomagnesemia had a statistically significant higher frequency of microalbuminuria. Our results were consistent with a study by Xu *et al*., which demonstrated an inverse relationship between serum magnesium and the prevalence of microalbuminuria.[23] Additionally, Gupta *et al*. found that T2DM patients with hypomagnesemia had an increased incidence of microalbuminuria [24]. It is unknown how precisely hypomagnesemia and microalbuminuria in DM relate to one another. Microalbuminuria is increasingly understood to be a result of oxidative damage [25]. It has been suggested that magnesium possesses antioxidant properties. In his study, Bakker AJ [26]. advised using ACR rather than urine albumin for microalbuminuria screening. But unlike UAC, the ACR demands more accurate sex- and age-specific discriminator values. According to a study by Alan R. Dyer *et al* [27]. based on their relative positives and negatives, both albumin concentration (UAC) and ACR seem to be a reasonable substitute for 24-hour albumin excretion. They suggested that UAC is an effective substitute for 24-hour albumin excretion for epidemiologic investigations where body size and weight measurements are difficult to obtain or where the added cost associated with measuring creatinine must be considered. One of the factors underlying the correlation between serum Mg and microalbuminuria may be oxidative stress. Depletion of magnesium is thought to decrease insulin sensitivity, raising the likelihood of subsequent problems [28]. 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. Microalbuminuria was reported to be prevalent among diabetics in studies by Janet Joy Kachuchuru Lutale *et al* [29]. Unnikrishnan R *et al* [30]. Thakkar B *et al* [31]. and Dayanidhi S *et al* [32] with prevalence rates of 10.7%, 26.9%, 54.09%, and 51%, respectively.

Our results were in line with those of a study by Bonakdaran *et al*., which likewise came to the conclusion that individuals with type 2 diabetes mellitus who had higher serum uric acid concentrations had a higher likelihood of developing albuminuria [33]. The last byproduct of adenosine's breakdown is uric acid, which is crucial to understanding the pathophysiology of insulin resistance [34]. Renal excretion, renal absorption, and uric acid synthesis can all be affected by hyperinsulinemia brought on by insulin resistance. Insulin resistance-related metabolic syndrome includes microalbuminuria as a key component [35].

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.

According to a study by Mokdad *et al* on Type 2 diabetes patients from 2001 [36] there is a link between obesity and microalbumin. They discovered a considerable correlation between microalbuminuria and patients with greater BMI. Similar investigations were also carried out by Dayanidhi S *et al* (2013) [37]. Onyechi Modebe *et al*.(2000) [38] Gall ma *et al*.(1997) [39]. and Phillips CA *et al*.(2002) [40]. They found a link between microalbuminuria and BMI that was positive.

When diabetic nephropathy develops, it is ultimately ineffective and refractory to treatment. It progresses as one of the progressive and persistent reductions in renal function. Additionally, the development of diabetic nephropathy renders the diabetic patient prone to atherosclerotic disease, a condition that frequently prevents diabetic patients from living longer, healthier lives even after receiving renal replacement therapy. In order to reduce the morbidity and mortality caused by the disease, it is obvious that the safest and most effective strategy for preventing diabetic nephropathy should focus on recognising and treating the condition at an early stage of development, or when it is thought to be more treatable.

Conclusion

It was concluded that, 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. It is necessary to conduct additional large-scale research and clinical trials on the impact of magnesium supplementation on diabetic complications in order to assess how hypomagnesemia and microalbuminuria are related.

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