Association of microalbuminuria and serum uric acid levels in patients with Type 2 diabetes mellitus

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ABSTRACT

Introduction: Microalbuminuria is associated with increased risk of progressive kidney disease, leading towards end-stage renal disease and cardiovascular morbidity and mortality in diabetic patients. Elevated serum uric acid is a feature of hyperinsulinemia/insulin resistance. Insulin normally promotes renal tubular sodium and uric acid reabsorption. In hyperinsulinemia (which occurs in insulin resistance), increased insulin levels lead to decreased excretion of uric acid by the kidneys. So, Serum uric acid increases due to impaired clearance. The interrelationship between uric acid levels and the onset or progression of microalbuminuria remains incompletely understood. The measurement of uric acid in laboratories is fast, simple, and affordable. So, this study was performed to assess the significance of microalbuminuria and uric acid in the early detection of renal and cardiovascular involvement in type 2 diabetes mellitus and early prevention of complications. **Methods:** A hospital-based cross-sectional study was conducted on 106 patients who had type 2 diabetes mellitus. Random spot urine and venous blood samples were collected, labelled, and stored. The urine microalbumin and serum level of uric were measured by nephelometry method using Mispa i3 and the spectrophotometry method using semi-automated analyzer Erba CHEM7. **Results:** There was a significant association of microalbuminuria with duration of diagnosis (p-value=0.001) while no association with age and gender. Similarly, there was a significant association of serum uric acid with duration of diagnosis (p-value=0.009) while no association with age and gender. There was a significant association of urinary microalbumin and serum uric acid in type 2 diabetes mellitus (p-value=0.001). **Conclusions:** The present study showed a significant association of microalbuminuria with the duration of diabetes. A significant association was observed between the duration of diabetes and development of micro and subsequently macroalbuminuria.

Keywords: Microalbuminuria, type 2 diabetes mellitus, uric acid.

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INTRODUCTION

Diabetes mellitus is a chronic metabolic condition characterized by hyperglycemia due to defects in insulin secretion, insulin action, or both. It leads to long-term damage, dysfunction, and failure of various organs, especially the eyes, kidneys, nerves, heart, and blood vessels.[1] Insulin is a hormone produced by the pancreas for the entry of glucose from the bloodstream to the body cells, where it is converted into energy or stored.[2] The main risk factors for the development of diabetes are ethnic differences, lifestyles, changes in eating preferences, and obesity.[3] Diabetes, if untreated, can cause macrovascular complications such as coronary artery diseases, peripheral artery diseases, stroke and microvascular complications such as diabetic nephropathy, neuropathy and retinopathy.[4] Globally, the prevalence of type 2 diabetes mellitus (T2DM) is 10.5%. An estimated 537 million adults aged 20 to 79 years worldwide have diabetes. By 2030, 643 million and by 2045, 783 million adults aged 20 to 79 years are projected to be living with diabetes.[2] The most serious health problem of diabetes mellitus is diabetic nephropathy

that most commonly leads to end-stage renal disease.[3] The leading cause of premature deaths in diabetics is diabetic nephropathy due to cardiovascular disease (CVD) as well as renal failure.[1] Diabetic nephropathy is a progressive kidney disease caused by damage to the capillaries in the kidney's glomeruli.[5] It is due to longstanding diabetes mellitus and is the prime reason for dialysis and is classified as a small blood vessel complication of diabetes.[6] Diabetic nephropathy has been classically defined by the presence of proteinuria >0.5 g/24h. This stage has been referred to as overt nephropathy, clinical nephropathy, proteinuria, or macroalbuminuria.[7] Microalbuminuria is a key indicator of the early stages of diabetic nephropathy. It is a common and well-established risk factor for macrovascular diseases in T2DM. Microalbuminuria represents the simplest and most sensitive prognostic factor to evaluate the risk of overt nephropathy in diabetes, representing the first stage of progressive diabetic renal disease.[8] Microalbuminuria is an early sign of impending nephropathy, which is defined as the urinary excretion of albumin at the rate of 30 to 300 mg/24 hour. This excretion of a small amount of albumin in the urine has been documented to predict renal failure and cardiovascular morbidity as well as mortality in diabetics.

The study has predicted that up to 30% of the people with newly diagnosed T2DM will already have abnormally high urinary albumin levels, and about 75.0% of these will have microalbuminuria.[1] The pathophysiological basis for elevated urinary albumin excretion entails the binding of glucose to proteins, resulting in excessive protein glycosylation with the buildup of advanced glycated end products. This leads to deposition of advanced glycated end products on the glomerulus, resulting in renal and glomerular hypertrophy, mesangial matrix accumulation and thickening of the glomerular basement membrane. This abnormality permits the leakage of low molecular weight proteins (albumin).[9] This is the stage of microalbuminuria (Incipient Nephropathy) which could be reversible with good glycemic control. However, with persistent microalbuminuria, further leakage of protein in urine will result in overt diabetic nephropathy. Increased level of microalbuminuria is associated with increased risk of progressive kidney disease, leading to end-stage renal disease and cardiovascular morbidity and mortality in diabetic patients, as reported in an earlier study.[10] Uric acid is a product of purine metabolism, and approximately two-thirds of it is excreted by the kidneys.[11] Elevated serum uric acid is a feature of hyperinsulinemia/insulin resistance.[12] Due to insulin resistance, there is glucose intolerance, high triglycerides, and low high-density lipoprotein. It results in congestive heart failure and hypertension, due to which the normal blood flow to the kidney for the elimination of uric acid gets disturbed. It results in a decreased GFR. So that results in elevated serum uric acid concentration.[13] The interrelationship between uric acid levels and the onset or progression of microalbuminuria remains incompletely understood. The measurement of uric acid in laboratories is fast, simple, and affordable.

So, this study was performed to assess the significance of microalbuminuria and uric acid in the early detection of renal and cardiovascular involvement in T2DM and early prevention of T2DM complications.

METHODS

This hospital-based cross-sectional study was conducted among the patients visiting endocrinology department of Gandaki Medical College Teaching Hospital and Research Center who were diagnosed with T2DM. The ethical clearance was obtained from the Institutional Review Committee (Ref. No.152/078/079). A written informed consent was taken from all the participants prior to data collection. A convenience sampling technique was used to enroll the participants in the study. A sample size of 106 was calculated.

Sample size: $n = \frac{z^2pq}{d^2}$

where; z = confidence interval at 95% (1.96)

p = prevalence value of microalbuminuria in Type 2 DM (7.5%).[14]

q = (1-p) = (1-0.075) = 0.925

d =error = 5% = 0.05

$$n = \frac{(1.96)^2 \times 0.075 \times 0.925}{(0.05)^2}$$

$$= \frac{3.84 \times 0.06}{0.0025}$$

$$= 106$$

All subjects visiting the outpatient department of GMCTHRC who were diagnosed with diabetes mellitus of age-group 20-79 years were involved in the study. The diagnostic criteria for diabetes mellitus were HbA1C of ≥6.5%, Fasting Blood Glucose (FBS) of ≥125 mg/dl and Post-Prandial Blood Glucose (PPBS) of ≥200 mg/dl. The patients with history of CVD events, Type 1 diabetes mellitus, urinary tract infection, on treatment with uric acid lowering drugs, hepatic or renal diseases and those refusing to be the part of study were excluded from the study.

Urine microalbumin: A random urine sample was taken for the estimation of urine microalbumin by the immunoturbidity principle using Mispa i3 instrument.

The reagents containing polyclonal goat anti-human microalbumin, when mixed with the urine sample containing microalbumin, agglutination occurs, which is directly proportional to the concentration of microalbumin in the sample.

Uric acid: A 2 ml venous blood sample was drawn aseptically from the patients. The blood sample was collected in plain vial tubes without anticoagulant, allowed to clot for 10 to 15 minutes. After clotting, the vial was centrifuged at 3000 rpm for 10 to 15 minutes to separate out serum. In case of delay, the vial was placed in the refrigerator to -20^0 Celsius. Serum uric acid was measured by the uricase enzymatic method in a semi-automated analyzer (spectrophotometry) using Erba CHEM 7.

The obtained data were entered in a Microsoft Excel sheet, and the statistical analysis was done using the Statistical Package for the Social Sciences (SPSS) 22.0 version.

RESULTS

This study was carried in 106 patients where, 70 were males (66%) and 36 were female (34%).

Table 1: Distribution of age group of respondents

Age	Male	Female	Frequency	Percentage
20-39	31	11	42	40%
40-59	30	18	48	45%
60-79	9	7	16	15%

Table 2: Distribution of respondents according to duration of diagnosis of T2DM

Duration of diagnosis	Frequency	Percent
<5 years	82	77%
≥5 years	24	23%

Table 2 shows the frequency of patients with the duration of diagnosis of type 2 diabetes mellitus.

Table 3: Association of microalbuminuria and serum uric acid

Variable		Serum uric acid		Chi-square	p-value
		≤7 mg/dl	>7 mg/dl		
Microalbuminuria	≤30 mg/l	64	6	19.711	0.001*
	>30mg/l	12	24		

*denotes statistical significance (p<0.05)

Table 3 shows the significant association of urinary microalbumin and serum uric acid in T2DM. (p value=0.001)

Table 4: Association of urinary microalbumin with age, gender and duration of diagnosis

Variables		Urinary microalbumin		Chi-square value	p-value
		≤30 mg/l	>30 mg/l		
Age	20-39	28	14	1.167	0.558
	40-59	34	14		
	60-79	8	8		
Gender	Male	46	24	0.005	0.945
	Female	24	12		
Duration of diagnosis	<5 years	68	14	23.03	0.001*
	≥5 years	2	22		

*denotes statistical significance (p<0.05)

Table 4 showed that there was a significant association of urinary microalbumin with duration of diagnosis (p value=0.001), while there was no association with age and gender.

Table 5: Association of serum uric acid with age, gender and duration of diagnosis

Variables		Serum uric acid		Chi-square value	p-value
		≤7 mg/dl	>7 mg/dl		
Age	20-39	30	12	0.463	0.793
	40-59	36	12		
	60-79	10	6		
Gender	Male	48	22	0.496	0.481
	Female	28	8		
Duration of diagnosis	<5 years	66	16	6.894	0.009*
	≥5 years	10	14		

*denotes statistical significance (p<0.05)

Table 5 shows the association of serum uric acid with age, gender, and duration of diagnosis. There was a significant association of serum uric acid with duration of diagnosis (p-value=0.009), while there was no association of serum uric acid with age and gender.

DISCUSSION

From the result of the research, it was shown that there was an association between urinary microalbumin and serum uric acid in T2DM. There was no association of urinary microalbumin with age and gender, while there was an association with the duration of diagnosis. No significant statistical relation was found between the microalbuminuria and the age of patients in our study. Our study was carried out in 106 patients, where 70 were males (66%) and 36 were females (34%) with a high frequency in males. A significant association was found between urinary microalbumin and serum uric acid in T2DM. Furthermore, there was a significant association between urinary microalbumin with duration of diagnosis, while there was no association with age and gender.

The study conducted in Pokhara by Sigdel et al. also showed the positive and strong correlation of microalbuminuria with duration of diagnosis.[1] This also supports our study. Similarly, the study conducted in Datta Meghe Medical College, Nagpur by Warjukar et al. also showed that there is a positive and significant correlation of microalbuminuria with duration of diabetes and serum uric acid in patients of diabetes mellitus.[3] A study conducted in Bir Hospital by Thakur et al. showed a statistically significant association between microalbumin and duration of diabetes mellitus.[14] The study conducted by Shrestha et al. showed microalbuminuria was significantly related to the duration of diabetes. No statistically significant relation was found between microalbuminuria and age.[15] Similarly, the study conducted in Kathmandu Medical College by Karki et al. showed microalbuminuria had a significant correlation with the duration of diabetes. This study was conducted for about six months with a small sample size. Some other parameters could be added in this study, such as Albumin Creatine Ratio, which could show the correlation between microalbuminuria and Albumin creatinine ratio in patients with T2DM.

CONCLUSIONS

The present study showed the association of microalbuminuria and uric acid with the duration of diabetes. This signifies that measurement of serum uric acid and microalbuminuria can help in the early detection of renal and cardiovascular involvement in T2DM and early prevention of its complications.

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AUTHORS' CONTRIBUTIONS

BG designed the research, collected data, performed statistical analysis, and prepared the first draft of the manuscript. SP and SP explained and interpreted the data and contributed to preparing the final draft of the manuscript. All authors read and approved the manuscript.

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