Original Research Article

A cross sectional study of correlation between serum uric acid level and micro-albuminuria in Type 2 Diabetes Mellitus patients

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Abstract

Background: Even though the role of serum uric acid as an early marker of diabetic nephropathy has been documented in many western studies, the amount of literature on the subject is very limited.
Objectives: To study the association between serum uric acid and micro-albuminuria in patients with Type 2 Diabetes Mellitus.
Materials and methods: The current study was a cross sectional study, conducted in the Department of Internal Medicine, Velammal medical college and hospital, which is a tertiary care teaching hospital. The study has included a total of 269 subjects with Type 2 DM, recruited by convenient sampling. Serum uric acid was measured by Direct Enzymatic Assay and urine micro albumin levels were measured by Latex Turbidimetric method. Association between the two variables was assessed by calculating pearson correlation coefficient and the data was represented in a scatter diagram.
Results: The mean age was 54.29 ±11.23 years and mean duration of diabetes was 4.85 years. Males outnumbered females by 2.84 times. There was a moderate, statistically significant correlation between HbA1 C level and serum uric acid in the study group (PCC=-0.353, p value < 0.001). There was a weak positive correlation between the blood urea levels and serum uric acid in the study group (PCC=0.145, P value 0.012). There was a weak, but statistically significant positive correlation between Hba1C values (PCC=0.170, p value 0.005), total cholesterol (PCC=0.180, p value 0.003), LDL cholesterol (PCC=0.165, p value 0.007) and urine micro albumin levels in study population. The

odds of micro albuminuria were 1.02 times (95% CI 0.58 to 1.79, p value 0.944) in people with uric acid between 5 to 7.49 and 1.855times (95% CI 0.56 to 6.081, p value 0.30) in patients with uric acid level of 7.5 and above, as compared to people with uric acid levels below 5 mg/dl.

Conclusions: Higher Hba1c levels were associated positively with elevated serum uric acid and micro albuminuria. Even though there is a weak positive correlation between the uric acid levels and micro albuminuria it was statistically not significant. The odds of micro albuminuria only slightly increased with increasing serum uric acid levels and duration of diabetes, but this association was statistically significant.

Key words

Type 2 Diabetes mellitus, Uric acid, Micro albumin.

Introduction

Nephropathy related to Diabetes mellitus (DM) is the commonest cause of end-stage renal disease in the developed countries and the number is growing each year [1]. World Health Organisation estimates that globally, about 422 million adults were diagnosed with diabetes in 2014, compared to 108 million in 1980 and the global prevalence of diabetes has nearly doubled since 1980, rising from 4.7% to 8.5% in the adult population [2]. Also over the past decade, prevalence of diabetes rose faster in low- and middle-income countries than in high-income countries.

The magnitude of impact of type 2 DM on kidney is such that nearly 25–40% of patients develop kidney damage and chronic kidney disease [3]. Additionally, among these patients, the risk of cardiovascular disease (CVD), the morbidity and premature mortality associated with DM and CKD is greatest with attendant economic burden on the individual and the country [4, 5].

The pathogenesis of nephropathy associated with diabetes is complex and still not well understood [6]. It has been postulated that it occurs as a result of the interplay of metabolic and hemodynamic factors in the renal microcirculation.

Evidence from numerous longitudinal studies have pointed that hyperuricemia is associated with an increased risk of cardiovascular events and death in both non-diabetic and type 2 DM individuals [7-10]. Hyperuricemia, an inflammatory factor, is found to be an independent predictor of vascular complications and mortality in patients with type 2 DM [11] and is associated with excess risk for development of diabetes [12, 13]. However, the relationship between diabetes mellitus and hyperuricemia is still subject to controversy.

On the other hand, micro-albuminuria is considered as the proxy of early stages of diabetic nephropathy and has been recognized as a marker of early glomerular and vascular damage [3]. There is an association of albuminuria and impaired glomerular filtration rate with more than normal serum uric acid (SUA) levels in type 2 DM patients [14]. The present study aimed to assess the relationship between SUA and albuminuria in type 2 DM patients.

Materials and methods

Study design: The study was a cross sectional study

Study setting: The study was conducted in the department of internal medicine, Velammal medical college and hospital, which is a tertiary care teaching hospital.

Study population: All the known and newly diagnosed cases of diabetes mellitus were included in the study.

Study duration: The study was carried out between July 2016 and December 2016.

Inclusion criteria

- Patients with Type 2 Diabetes mellitus
- Adult population > 20 years of age, belonging to both genders

Exclusion criteria

- Patients with elevated renal parameters and gout were excluded

Study procedure: Serum uric acid was measured by Direct Enzymatic Assay and urine microalbumin levels were measured by Latex Turbidimetric method.

Ethical considerations: The study was approved by institutional human ethics committee. Informed written consent was obtained from all study participants. Confidentiality of the study participants was maintained throughout the study.

Statistical methods:

Urine micro albumin was considered as the primary outcome variable. Serum uric acid was considered as primary explanatory variable. Duration of diabetes mellitus, age of the patient, glycemic control as assessed by Hba1C levels, lipid profile parameters were considered as explanatory variables. Descriptive analysis was carried out by mean and standard deviation for quantitative variables, frequency and proportion for categorical variables. Data was also represented using appropriate diagrams like bar diagram, pie diagram and box plots. Association between quantitative explanatory and outcome variables was assessed by calculating Pearson correlation coefficient and the data was represented in a scatter diagram. P value < 0.05 was considered statistically significant. IBM SPSS version 22 was used for statistical analysis [15].

Results

A total of 269 patients were included in the final analysis. The mean age of the study participants was 54.29 ±11.23 years. Males outnumbered females by 2.84 times in the study population. The mean duration of diabetes was 4.85 years. Among the total, 60.59% were known cases of diabetes and remaining 39.41% were diagnosed recently (< 1 year). The proportion of current smokers and alcoholics was 17.84% and 24.91% respectively. Known hypertensive constituted 29% and another 14.87% were recently diagnosed with hypertension. The mean HbA1c level in study population was 7.53 %. The mean values of lipid profile parameters, blood urea and serum creatinine were within normal physiological limits. The mean serum uric acid level was 4.95±1.48 and the mean urine micro albumin level was 34.56± 71.39 in study population (**Table - 1**).

Table - 1: Descriptive analysis of socio demographic parameters in study group (N=269).

Parameter	Summary
Age (mean ±SD)	54.297 ± 11.23
Male : Female Ratio	2.84:1
Duration of diabetes (mean ±SD)	4.845 ± 6.51
Diabetes History	
Known Case	163(60.59%)
Recently Diagnosed	106(39.41%)
Smoking status	
• Past	23 (8.55%)
• Current	48(17.84%)
Alcohol Status	
• Past	23(8.55%)
• Current	67(24.91%)
Hypertension	
Known Case	78 (29%)
Recently Diagnosed	40(14.87%)
HbA1c	7.536 ± 1.843
Total Cholesterol	190.4 ± 46.60
HDL	40.24 ± 8.110
LDL	118.8 ± 37.33
TGL	118.8 ± 139.4
Blood Urea	22.28 ± 7.544
Serum Creatinine	0.805 ± 0.225
Uric Acid	4.955 ± 1.482
Urine Micro albumin	34.56 ± 71.39

There was a moderate, statistically significant correlation between HbA1 C level and serum uric

acid in the study group (PCC=-0.353, p value < 0.001). There was a weak positive correlation between the blood urea levels and serum uric acid in the study group (PCC=0.145, P value 0.012). The other factors had shown no statistically significant correlation with serum uric acid in the study group (**Table - 2**).

Table - 2: Correlation between various diabetes related parameters and Serum Uric Acid in study group.

Parameter	Pearson Correlation Coefficient(PCC)	P value
Age	0.021	0.737
Duration of diabetes	0.013	0.838
HbA1c	-0.353	***<0.001***
Total Cholesterol	0.023	0.706
HDL	-0.048	0.434
LDL	-0.028	0.644
TGL	0.043	0.482
Blood Urea	0.152	***0.012***

There was a weak, but statistically significant positive correlation between Hba1C values (PCC=0.170, p value 0.005), total cholesterol (PCC=0.180, p value 0.003), LDL cholesterol (PCC=0.165, p value 0.007) and urine micro albumin levels in study population. Other factors had shown no statistically significant association with urine micro albumin in the study group (**Figure – 1**, **Table – 3**).

The odds of micro albuminuria was 1.02 times (95% CI 0.58 to 1.79, p value 0.944) in people with uric acid between 5 to 7.49 and 1.855 times (95% CI 0.56 to 6.081, p value 0.30) in patients with uric acid level of 7.5 and above, as compared to people with uric acid levels below 5 mg/dl (**Figure – 2**).

Then compared to people with diabetes for less than 5 years, the odds of micro albuminuria was 1.21 (95% CI 0.56 to 2.62, p value 0.622) and 1.16 times (95% CI 0.50 to 2.68, p value 0.718) in patients with duration of diabetes 6 to 10 years and > 11 years respectively (**Table - 4**).

Table - 3: Correlation Between Various Diabetes Related Parameters and Urine Micro Albumin in Study Group.

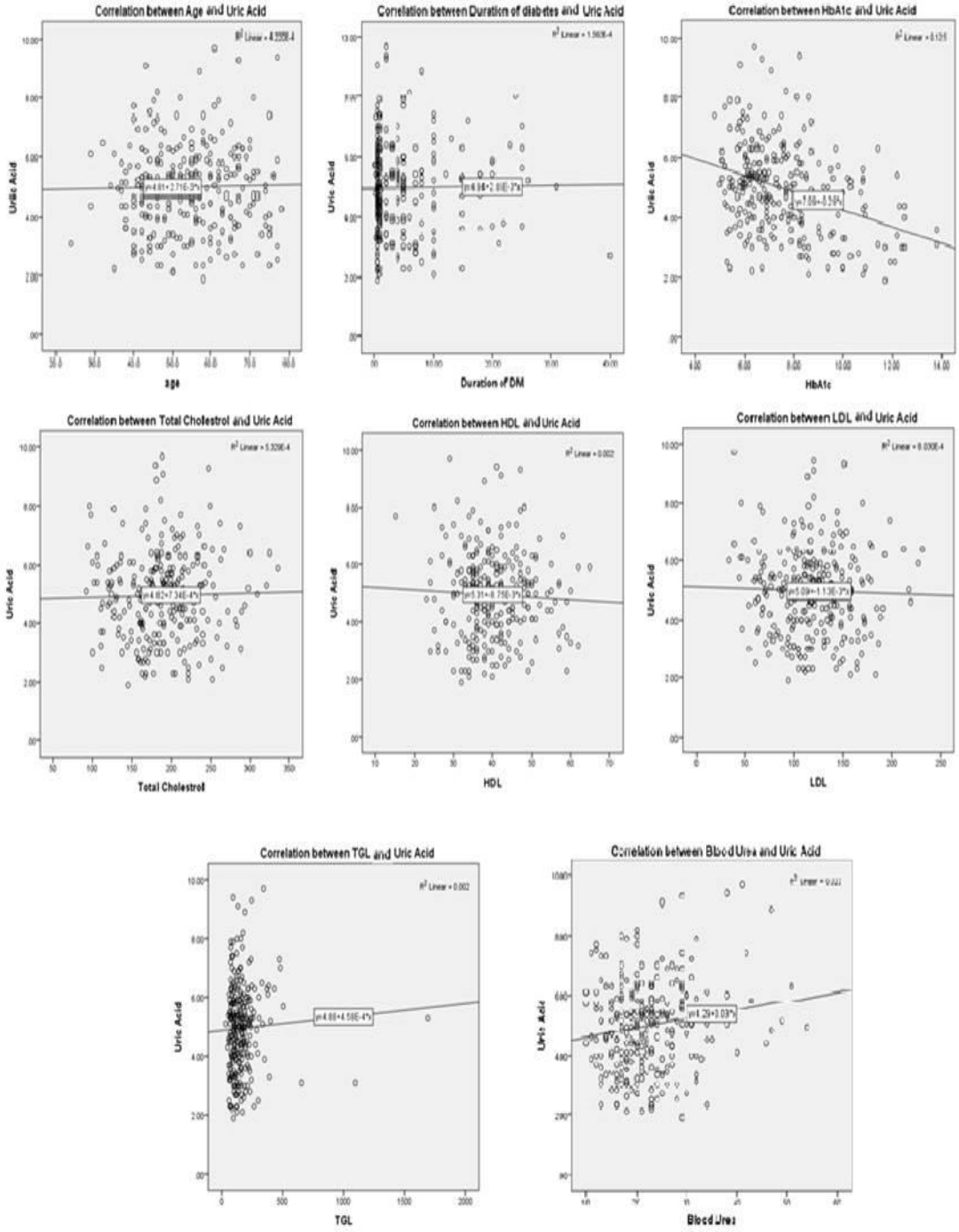
Parameter	Pearson Correlation Coefficient (PCC)	P value
Age	-0.103	0.091
Duration of diabetes	0.099	0.104
Hba1c	0.170	0.005
Total Cholesterol	0.180	0.003
HDL Cholesterol	-0.054	0.380
LDL Cholesterol	0.165	0.007
TGL	0.109	0.074
Blood Urea	0.048	0.438
Uric Acid	-0.001	0.984

Discussion

Uric acid, the end product of purine catabolism in humans is an anti-oxidant and has long been hypothesized that it might protect against oxidative stress or cell injury and ageing [16]. However, paradoxically the anti-oxidants can become pro-oxidant compounds in certain situations, particularly when they are present in blood at above normal levels. In line, current epidemiological studies have found an association between elevated SUA concentration and increased albuminuria [17-21], owing to the endothelial damage caused by SUA [21].

The present study findings revealed that mean SUA level was 4.95 mg/dl. A similar SUA value was reported by Suzuki K et al, (5.1 mg/dL) [22]. Also raised hyperuricemia significantly increases chronic micro/macro vascular complications in type2 DM other chronic vascular complications like coronary artery disease, cerebrovascular disease, diabetic retinopathy and peripheral neuropathy [19].

Figure - 1: Correlation between various diabetes related parameters and Serum Uric Acid.



There is mounting evidence associating albuminuria and SUA in type2 DM patients [23-26]. However, several of these studies are cross-sectional in design and very few of such studies assessed whether a high-baseline serum uric acid predicts development of microalbuminuria [20]. The mechanism of SUA influencing albuminuria is that the increased SUA induce glomerular damage that in turn leads to albuminuria, which also increases the urinary albumin-creatinine ratio [22].

Contrasting with the findings of several large-scale studies, there was a moderate but significant correlation between HbA1c level and serum uric acid in the study group (PCC=-0.353, p value < 0.001). The US Third National Health and Nutritional Survey (NHANES III) during

1988-94 assessing 14664 individuals found a bell-shaped relation of fasting glucose levels with serum uric acid levels. Individuals with diabetes showed lower serum uric acid levels and the association was larger among men (p-value for interaction, 0.007).

Figure - 2: Correlation between Diabetes Related Parameters and Urine Micro-Albumin.

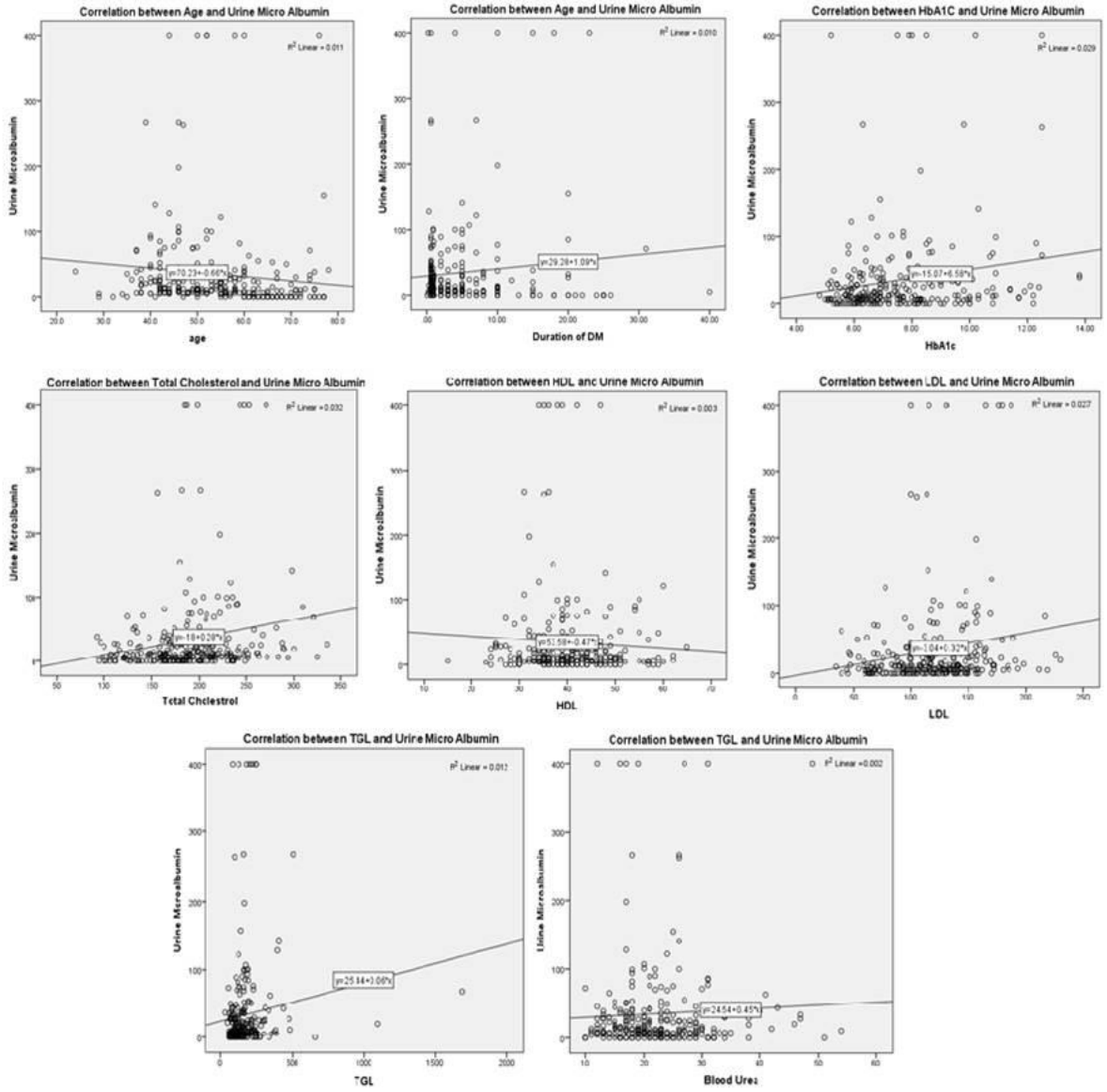


Table - 4: Univariate Logistic Regression Analysis of Factors Influencing Micro Albuminuria.

Parameter	Unadjusted odds ratio	95% CI of odds ratio		P value
		Lower	Upper	
Serum Uric acid (baseline =Below5)				
5 to 7.49	1.021	.581	1.792	0.944
7.5 and above	1.855	.566	6.081	0.30
Duration of diabetes (Baseline =< 5)				
6 to 10	1.214	.562	2.624	.622
> 11	1.166	.506	2.686	.718

There was a weak positive correlation between the blood urea levels and serum uric acid in the study group (PCC=0.145, P value 0.012).

There was a weak, but statistically significant positive correlation between Hba1C values (PCC=0.170, p value 0.005), total cholesterol (PCC=0.180, p value 0.003), LDL cholesterol (PCC=0.165, p value 0.007) and urine micro albumin levels in study population.

Urine micro-albumin was found to be 34.56mg/L. Contrastingly the micro-albumin was less in the studies of Wu D, et al., (22.32 mg/dL) [27]. The presence of urinary albumin was significant across the age groups ($p<0.05$) and males had significantly higher albuminuria than females ($p<0.05$). Evidence suggests that both elevated uric acid and microalbuminuria levels were significantly associated with diabetic chronic micro/macro-vascular complications. Monitoring of their levels provides a predictive value for a presence of chronic micro/macro-vascular complications in patients with type 2 DM [11, 19, 28, 29].

Conclusions

Higher Hba1c levels were associated positively with elevated serum uric acid and micro albuminuria. Even though there is a weak positive correlation between the uric acid levels and micro albuminuria it was statistically not significant. The odds of micro albuminuria only slightly increased with increasing serum uric acid levels and duration of diabetes, but this association was statistically significant

Limitations

Considering the lower effective sample size, the study could not assess the relative contribution of various influencing factors on microalbuminuria by multivariate analysis

Recommendations

- Large scale prospective studies to assess the association of uric acid with subsequent development of micro albumuria needs to be conducted
- The effect of any interventions to reduce the uric acid levels on micro albuminuria also needs to be explored

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