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Original Article

A study to find out the correlation between urine microalbumin and serum uric acid levels among type-2 diabetic patients with nephropathy

Priyanka Ramakrishnan [1], Santhini Gopalakrishnan [2] *

[1] Chettinad Academy of Research and Education, Chennai, India

[2] Department of Biochemistry, Chettinad Hospital & Research Institute, Chennai, India

* Correspondence to: Santhini Gopalakrishnan, Department of Biochemistry, Chettinad Hospital & Research Institute, Chennai, India. Phone: +91 7299069636; E-mail: santhini.research@gmail.com

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Abstract

Diabetic nephropathy is one of the most common complications of diabetes mellitus. Early detection of the complication is required for proper effective and timely treatment. This article aims to determine the role of serum uric acid and microalbumin levels in diagnosing diabetic nephropathy. We collected the data from 100 cases with diabetic nephropathy and 100 with diabetes but without nephropathy controls. Fasting plasma glucose, postprandial blood glucose, uric acid, blood urea nitrogen (BUN) and creatinine levels, microalbumin and eGFR levels were assessed in all the subjects. As a result, the independent sample t-test showed a significant difference in the levels of FBS, BUN, creatinine, uric acid and microalbumin levels among cases and controls (p-value<0.05). Pearson correlation showed a significant positive correlation between serum uric acid and microalbumin. ROC curve showed AUC for HbA1c, serum uric acid and microalbumin as 0.814, 0.713 and 0.706, respectively. In conclusion, serum uric acid can be used as a biomarker for the early detection of diabetic nephropathy.

Keywords: diabetic nephropathy, uric acid, microalbumin.

Introduction

By 2025, the global prevalence of adults with diabetes will be 5.4 percent. One of the most widespread causes of chronic renal failure is diabetic nephropathy [1]. It is a significant kidney consequence of type 2 diabetes.

Age, diabetes duration, hypertension, and HbA1c levels are only a few of the risk variables that have been linked to the development of diabetic nephropathy. Creatinine is one of the most popular analytes used to determine GFR and renal function.

Microalbuminuria is defined as a ratio of 30 to 300, while macroalbuminuria is defined as a ratio of more than 300. Microalbuminuria occurs 10–14 years prior to the onset of overt diabetic nephropathy. At this point, diabetic kidney disease may be reversed or prevented from worsening.

Uric acid has also been implicated in pathways that contribute to nephropathy. Several studies have revealed a link between high uric acid levels and the development of diabetic nephropathy [2].

Purine bases metabolism produces uric acid as a by-product. In high-level conditions, uric acid penetrates the cell and serves as an oxidant, acting as a separate risk factor for nephropathy prediction. Increased uric acid causes platelet adhesion and aggregation, which favors vascular thrombosis [3].

Despite current treatments, the risk of chronic kidney disease in diabetics cannot be completely eliminated.

Study of new biomarkers, developing systematic random clinical trials (RCT) that derive accurate and relevant results in order to develop appropriate therapeutic agents and treatment modalities that target kidney-specific disease mechanisms like inflammation,

glomerular filtration and fibrosis are important to achieve the goal of improving health outcomes and better curative results.

Hence timely assessment of serum uric acid and urine microalbumin as markers can be used to find out the extent of damage in chronic kidney disease patients with nephropathy as a definitive predictive, prognostic, and diagnostic marker at the very beginning of its hint of progression to avoid such sequelae and progression for a multidisciplinary targeted approach analysis and treatment of the patient (Figure 1).

Aim

To analyze serum uric acid (UA) and urine microalbumin as a marker of renal injury in type 2 diabetes mellitus. To determine the correlation between serum uric acid concentrations and urinary microalbumin concentrations in subjects with diabetic nephropathy. To analyze the microalbumin and uric acid levels in the different stages of Diabetic Nephropathy.

Material and methods

Two hundred subjects with Type 2 diabetes of both genders between the age groups of 40–70 years are diagnosed using the American Diabetic Association (ADA) guidelines [Fasting Blood Sugar (FBS) >126 mg/dl, Post Prandial Blood Sugar (PPBS) ≥200 mg/dl] in the General medicine OPD and ward of Chettinad health and research institute were taken up for the study.

Subjects were divided into two groups based on the microalbumin levels into nephropathy and non-nephropathy groups. The subjects having microalbumin levels less than 30 mg/dl were taken as controls (non-nephropathic group) and the microalbumin levels between 30–300 mg/dl were taken as cases (nephropathic group).

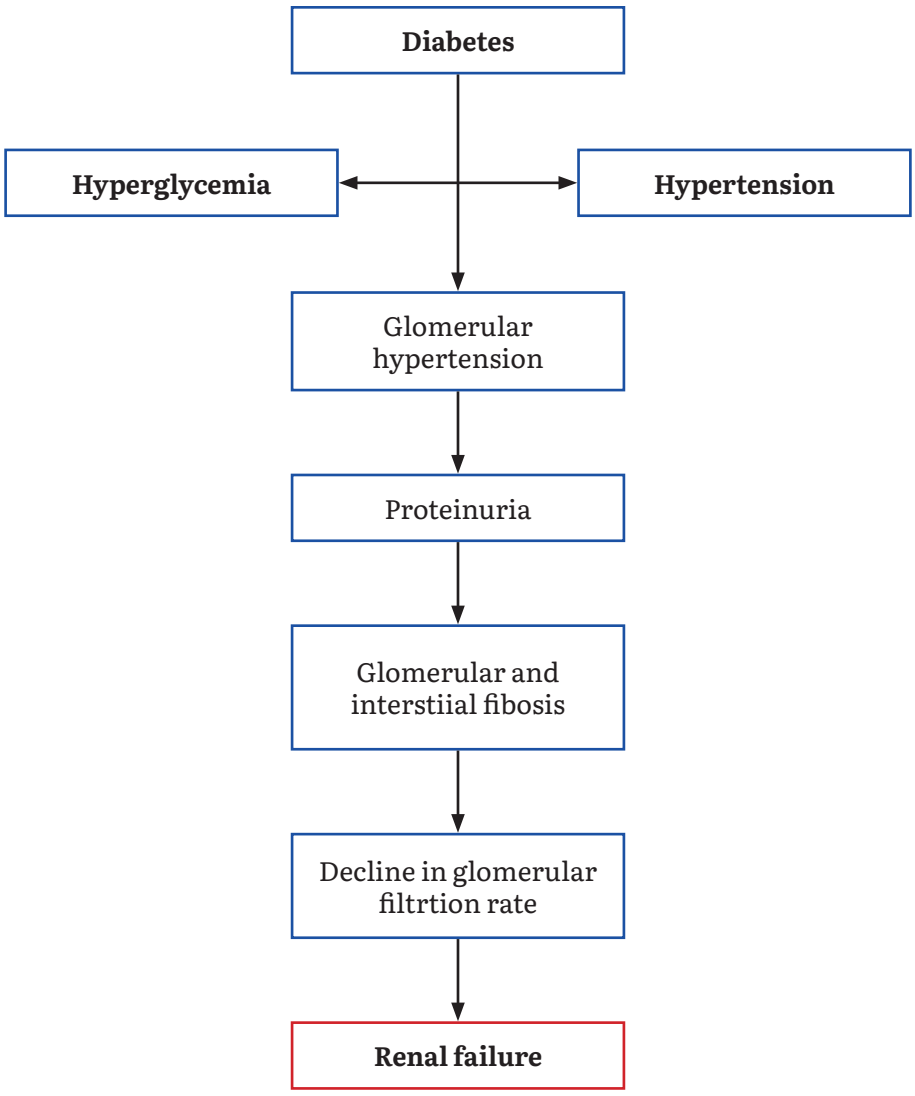

Figure 1: Pathogenesis of diabetic nephropathy.

Out of the 200 patients, the study population comprised of two groups, 100 cases and 100 controls, who participated in the study.

Exclusion criteria

Patients with H/O Gout, allopurinol or thiazide diuretics intake, urinary tract disease, malignant conditions and congenital disorders associated with elevated uric acid, liver diseases, pregnancy, kidney transplantation, malignancy, nephrotoxic drugs intake, anti-inflammatory drugs intake were excluded from the study.

The Institute's Ethics Committee approval was obtained prior to the commencement of the study. After obtaining consent, the subject's gender, age, body mass index (BMI), waist circumference, duration of diabetes, systolic blood pressure, and diastolic blood pressure were recorded.

Five milliliters of blood was obtained from each of the subjects in red topped vacutainers for analyzing the uric acid, blood urea nitrogen (BUN) and creatinine levels, grey topped vacutainers for fasting blood sugar (FBS) and postprandial blood sugar (PPBS), violet topped vacutainers for HBa1c levels. A spot urine sample was collected to analyze the levels of microalbumin. All the samples were analyzed on the same day and the various parameters' levels were obtained.

Serum uric acid levels were measured by the URCA method, a modification of the uricase method by colorimetric analysis.

eGFR (estimated glomerular filtration rate) was calculated using the Modification of Diet in Renal Disease Study (MDRD) formula:

$$[186 \times (\text{Creatinine}/88.4)^{-1.154} \times (\text{Age})^{-0.203} \times \\ \times (0.742 \text{ if female}) \times (1.210 \text{ if black})]$$

FBS, PPBS, urea, BUN, creatinine, uric acid and microalbumin levels were measured using the Siemens RXL machine auto analyzer and HbA1c in D10 machine in the Central Lab of the biochemistry of Chettinad hospital and research institute.

Results

The data were analyzed using the SPSS software, version 26. The analysis of Hba1c, uric acid, microalbumin, BUN, fasting blood glucose and postprandial glucose in 100 cases and 100 controls was done.

Descriptive statistical analysis was done to determine the mean and standard deviation of all the parameters (Table 1).

An independent sample t-test was done to compare the values between the cases and controls. P-value <0.05 will be considered to be statistically significant. There was a significant difference in the values of FBS, BUN, creatinine, uric acid and urine microalbumin levels. We found a significant difference in the values of uric acid (p-value=0.001), urine microalbumin (p-value=0.001), fasting blood glucose (p-value=0.001), creatinine (p=0.001), BUN (p-value=0.002) (Table 2).

Pearson's correlational analysis was done and a significant correlation was found between serum uric acid levels and urine microalbumin levels in the cases (Table 3). The ROC curve was done to analyze the specificity and sensitivity of HbA1c, serum uric acid and urine microalbumin levels. The area under the curve was found to be 0.814, 0.713 and 0.706, respectively. (Figure 2, Table 4).

Discussion

Diabetic nephropathy is the most widespread and a leading cause of chronic kidney failure among type 2 diabetic patients. With the rising number of cases, it is more important than ever to make an early, accurate

Table 1: Shows the descriptive statistics of all analytes.

	Descriptive statistics				
	N	Minimum	Maximum	Mean	Std. Deviation
AGE	200	21.0	87.0	53.830	12.2319
FBS	200	92	435	182.68	71.948
PPBS	200	82	668	265.50	110.804
Hbalc	200	3.2	7.3	4.625	.6428
BUN	200	3	23	11.07	3.882

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Table 1: Continued.

	Descriptive statistics				
	N	Minimum	Maximum	Mean	Std. Deviation
Creatinine	200	.42	1.81	.9082	.24678
Uric acid	200	2.1	8.5	4.718	1.1683
Urine microalbumin	200	1.00	212.00	43.7043	45.19484
Egfr	200	161.4	34.4	82.625	23.477

Table 2: Independent sample t-test done between the parameters in cases and controls (p-value<0.05 is considered significant).

	CASES		CONTROLS		P-value
	Mean	Standard Deviation	Mean	Standard Deviation	
FBS	203.06	81.733	162.30	53.721	0.001
PPBS	290.94	120.140	240.07	94.542	0.112
Hba1c	4.518	.5351	4.732	.7219	0.662
BUN	11.59	4.207	10.54	3.468	0.002
Creatinine	.8990	.28259	.9174	.20589	0.001
Uric acid	4.436	1.1241	7.001	1.1483	0.001
Urine microalbumin	76.7054	43.14042	10.7031	6.67308	0.001
eGFR	83.842	26.572	81.869	19.996	0.5537

and timely diagnosis to prevent organ failure and improve the patient's prognosis.

Currently, the staging of diabetic nephropathy is mainly based on urine microalbumin levels as a spot urine sample, either as the first urine in the morning or as a random sampling along with eGFR calculation and other renal parameters.

We compared and assessed the correlation between serum uric acid and urine microalbumin among type-2 diabetic patients to evaluate uric acid as a marker for diabetic nephropathy in this study. Our study revealed a statistically significant positive correlation between serum uric acid levels and urine microalbumin and revealed that the levels of serum uric acid increased with an increase in levels of urine microalbumin.

Our results are on par with the studies done by Mehmet *et al.*, who did a study among 100 patients with Type-2 diabetes mellitus. They were separated into nephropathy and non-nephropathy groups, with the diabetic nephropathy group showing an increase in serum uric acid compared to the non-nephropathy group, and the levels of uric acid also increased with an increase in microalbumin, which was statistically significant [4]. Another study by Li. G *et al*. examined the relationship between type 2 diabetes progression and blood uric acid levels in 50 patients with nephropathy who had type 2 diabetes. BUN, creatinine Hba1c, lipid profile, and uric acid were evaluated. Serum HDL levels were significantly lower, creatinine was higher, LDL and total cholesterol levels were higher and multiple linear

Table 3: Shows the Pearson correlation analysis between the parameters (p-value<0.05 is considered significant).

	HbA1c	Uric acid	Microalbumin
Hba1c	1	0.955 (0.001)	0.310 (0.002)
Uric acid	0.955(0.001)	1	0.327(0.001)
Microalbumin	0.310(0.002)	0.327(0.001)	1

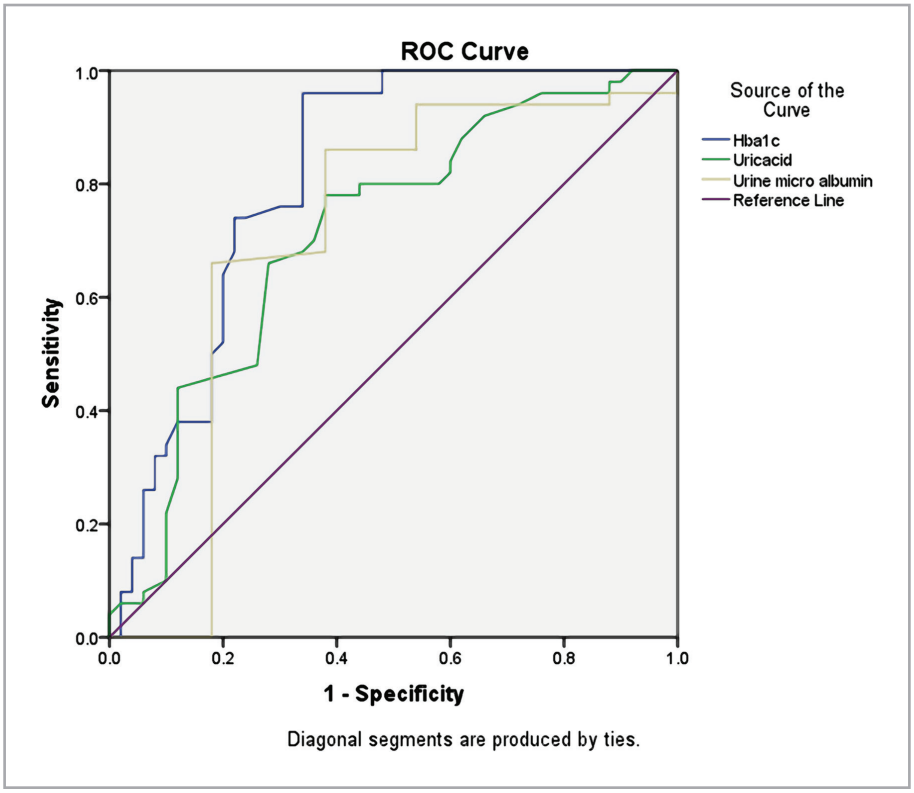

Figure 2: Shows the ROC CURVE ANALYSIS OF HbA1c, serum uric acid and urine microalbumin.

regression analysis revealed that uric acid levels were a risk factor for diabetic nephropathy progression [5].

Uric acid increases inflammation, oxidative stress and endothelial dysfunction of the glomerular capillaries along with activation of thrombus formation and RAAS system leading to kidney dysfunction and aggravating the symptoms of nephropathy in type-2 diabetes.

In a study by Ritah Kiconco *et al.*, a cross-section of a study involving 140 participants with diabetes mellitus from a population in South Western Uganda was done to assess the efficiency of uric acid as a traditional renal marker. There was also a statistically significant positive correlation between microalbumin and uric acid levels [6]. Danii Ls Suijk *et al.* reported that plasma uric acid was connected to elevated renal arterial afferent tone causing renal injury through ischemia by measuring effective renal vascular resistance in 88 white men and women with type-2 diabetes in the Amsterdam community between the ages of 58 and 68 [7].

Increased serum uric acid levels are thus associated with high urinary kidney injury molecules-1 and pro-inflammatory cytokines, causing extensive kidney damage. According to a study conducted by Naiara S. Guarda *et al.*, 125 patients with type-2 diabetes were divided into two groups based on uric acid levels in the Brazilian population [8]. Increased levels of serum uric acid are produced with an increase in purine metabolism due to oxidative damage and stress, which damages the kidney cells, causing renal failure.

However, Li Li *et al.* conducted a study with 409 obese Chinese people. The findings revealed that serum

Table 4: Analysis of the area under the curve.

The area under the curve	
Test result variable(s)	**Area**
Hbalc	.814
Uric acid	.713
Urine microalbumin	.706

Note: The test result variable(s): Hbalc, Uric acid, Urine micro albumin has at least one tie between the positive actual state group and the negative actual state group. Statistics may be biased.

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uric acid did not correlate with microalbumin levels or any metabolic disease, such as type 2 diabetes mellitus [9].

Though urine microalbumin is the currently available marker for assessing the severity of diabetic nephropathy, it has its own disadvantages in terms of cost and is the only method for diagnosis with no supporting marker for additional confirmation. Uric acid serves the purpose as a cheaper alternative and an effective additional marker for timely and periodic assessment of staging and severity of diabetic nephropathy.

Furthermore, studies with a larger sample size are necessary to effectively establish a stronger relationship between serum uric acid and urine microalbumin and to develop protocols and confirmatory diagnostic criteria for diagnosing diabetic nephropathy.

Conclusion

From this study, we infer that there is a significant difference in the uric acid levels between cases and controls. Also, there is a statistically significant positive correlation between serum uric acid levels and urine microalbumin levels. Hence, uric acid can be used as a biomarker for early diagnosis of diabetic nephropathy.

Acknowledgments

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Conflict of interest

The authors declare no conflict of interest.

Ethics approval

The approval for this study was obtained from the Ethics Committee of the Chettinad Academy of Research and Education-Institutional Human Ethics Committee (approval ID: 189/IHEC/November2020).

Consent to participate

Written informed consent was obtained from the participants.

Founding

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