



Comparison of clinical biochemistry indices between type 2 diabetic patients with nephropathy and non-nephropathy

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Abstract

Background: Diabetic nephropathy is a major cause of kidney failure. The current study aimed to measure serum and urine albumin, as well as other biochemical markers, in individuals with type 2 diabetic nephropathy and to identify rapid diagnostic approaches in these patients.

Methods: This case-control study included 40 patients with diabetic nephropathy and 40 diabetic patients without nephropathy as the control group. Clinical parameters were assessed. After biochemical analysis and based on the ratio of random urine albumin to creatinine, patients were divided into two groups: those without albuminuria and those with microalbuminuria. SPSS version 18 software was used to analyze the results.

Results: In diabetic patients, the levels of urea, creatinine, and uric acid were significantly higher compared with the control group and were 64.68 ± 46.84 , 2.01 ± 1.82 , and 5.35 ± 2.23 , respectively. The average serum albumin content in diabetic patients with nephropathy was notably lower than that in patients without nephropathy (3.74 ± 0.88 and 4.35 ± 0.28 , respectively) ($p < 0.05$). In patients with diabetic nephropathy, urinary albumin had a direct relationship with serum creatinine level ($r = 0.347$, $p = 0.028$). In the control group, serum albumin status could be assessed by measuring creatinine ($r = -0.305$, $p = 0.056$), urea ($r = -0.333$, $p = 0.036$), and HbA1C ($r = -0.376$, $p = 0.017$).

Conclusion: The results of this study revealed that high urinary albumin levels in patients with diabetic nephropathy have a direct association with serum creatinine levels, indicating a useful marker for evaluating nephropathy patients with albuminuria. However, further studies with larger numbers of participants are required.



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Introduction

Because of rapid population growth, aging, urbanization, and increases in obesity and physical inactivity, type 2 diabetes has rapidly become a global health problem. As a result, immediate action is required to prevent diabetes and its complications. The global prevalence of diabetes is expected to increase from 4% in 1995 to 5.4% by 2025 (1). The most common reasons for patient admission are acute and chronic diabetic complications (2). Diabetes is the leading cause of kidney failure, accounting for over 44% of new cases (3). Even if diabetes is well managed, it can result in chronic kidney disease (CKD) and renal failure (RF). Diabetic nephropathy is found in 30.3% of CKD patients, followed by chronic interstitial nephritis (23%) and chronic glomerulonephritis (17.7%) (4). Diabetic nephropathy (DN) is a type of kidney disease caused by diabetes. Nephropathy is the major cause of chronic renal failure globally, accounting for approximately one-third of renal failure cases among dialysis patients (5).

Serum albumin is the most prevalent intravascular protein and is commonly used in the laboratory for disease diagnosis. This protein is a crucial molecule in regulating osmotic pressure and acts as a carrier of medicines, fatty acids, and metals (6). Microalbuminuria occurs when small amounts of blood albumin leak into the urine in persons with renal impairment. As the amount of microalbuminuria increases, the filtration function of the kidney declines, resulting in high blood pressure. High blood pressure may worsen kidney damage (7). Albuminuria has also been demonstrated to be a good predictor of poor renal outcomes in patients with type 2 diabetes and hypertension (8). Patients with serum albumin levels less than 3.5 g/dL have an increased risk of renal problems. When serum albumin decreases from 3.5 to 3 g/dL, the mortality rate in patients with renal disorders increases by 15% (9).

Furthermore, some studies have found a clear link between glycemic control and microalbuminuria (10). Sheng et al. demonstrated that microalbuminuria is mostly caused by high diastolic blood pressure and plasma glucose levels (11). Thus, in diabetic patients, the HbA1C index is regarded as a predictive factor for diabetic peripheral neuropathy and cardiovascular autonomic neuropathy (12,13). Accurate glycemic control is critical in the diabetic population because it minimizes microvascular and macrovascular consequences in patients with type 1 and type 2 diabetes.

Consequently, the importance of diagnosing the stage of diabetes and preventing diabetes complications led to the design of this research to investigate the association of different biochemical markers, such as serum and urine albumin, in diabetic patients with or without nephropathy. Additionally, these findings could support rapid diagnostic and management approaches in these individuals and hopefully assist treatment strategies.

Methods

In this case-control study, which was approved by the Research Ethics Committee of Golestan University of Medical Sciences (Approval Code: IR.GOUMS.REC.1401.158), 80 patients with type 2 diabetes (40 without nephropathy and 40 with nephropathy) were randomly selected and included after receiving a final diagnosis from an endocrinology specialist. In addition, patients were requested to provide informed consent. A checklist was used to collect demographic information. Whole blood samples (10 mL) and urine samples were collected from both groups. The whole blood and urine samples were then sent to the Metabolic Disorders Center, Golestan University of Medical Sciences, Gorgan, Iran, for biochemical analysis.

After centrifugation and serum separation, spectrophotometric methods using PARS AZMUN kits were used to determine albumin, uric acid, urea, serum creatinine, urine albumin and PISHTAZ TEB for blood hemoglobin A1C. The measurement was done as the instructions of each kit with their reagents and then the absorbance was read in favored wavelength with spectrophotometer.

Inclusion and exclusion criteria

Inclusion criteria included age over 35 years, confirmed diagnosis of type 2 diabetes and duration of diabetes by an endocrinology specialist, and consent to participate in the study. In addition, patients with urinary tract infections, underlying kidney problems (Other than diabetic nephropathy) and renal vascular problems, heart failure, one kidney, pregnancy, type 1 diabetes, lack of blood pressure, hematuria, urinary specific gravity less than 1015, a history of using diuretics and drugs causing proteinuria, and dialysis were excluded from the study.

Statistical analysis

The examined variables were analyzed using descriptive statistics, such as mean, standard deviation, frequency, percentage, and statistical charts (Using SPSS software version 18). Pearson's correlation was used to assess the correlation of chemical parameters with serum albumin or urine albumin (Uric acid, HbA1C, creatinine, and urea). In addition, to compare the above parameters between the two groups of patients, the T-test was used in cases of normal data distribution and the Mann-Whitney test in cases of non-normal data distribution. A p-value of less than 0.05 was deemed significant.

Results

Biochemical markers were evaluated in 80 participants with type 2 diabetes in this study. There were 40 individuals with diabetic nephropathy and 40 patients without nephropathy as the control group. The average age of all patients was 61.48 ± 11.52 . Table 1 shows other demographic and clinical biochemistry factors, such as serum and urine albumin, urea, creatinine, and uric acid levels.

Due to the non-normal distribution of quantitative data according to the Shapiro-Wilk test, the Mann-Whitney test was used to compare the average serum levels of laboratory and biochemical parameters in patients with and without diabetic nephropathy, and the results showed a significant difference between the two groups ($p = 0.0001$). In addition, there was a significant difference in serum and urine albumin between the two groups ($p = 0.0001$).

Table 1. Biochemical factors measured in diabetic patients; values are reported as Mean $\pm$ SD

Variable (Unit)	Diabetic patients		Total	P-value
	Nephropathic	Non-nephropathic		
Age (Year)	60.72 $\pm$ 11.37	62.23 $\pm$ 11.76	61.48 $\pm$ 11.52	0.564
BMI (kg/m ²)	29.15 $\pm$ 4.29	28.08 $\pm$ 4.89	28.61 $\pm$ 4.60	0.301
HbA1C (%)	6.72 $\pm$ 0.97	7.66 $\pm$ 1.45	7.19 $\pm$ 1.32	0.0001
Urea (mg/dL)	90.94 $\pm$ 53.08	38.44 $\pm$ 14.62	64.68 $\pm$ 46.84	0.0001
Creatinine (mg/dL)	1.82 $\pm$ 2.01	1.02 $\pm$ 0.60	2.00 $\pm$ 1.82	0.0001
Uric acid (mg/dL)	5.35 $\pm$ 2.23	3.99 $\pm$ 1.13	5.35 $\pm$ 2.23	0.0001
Serum albumin (g albumin/dL)	3.74 $\pm$ 0.88	4.35 $\pm$ 0.28	3.74 $\pm$ 0.88	0.0001
Urine albumin (mg albumin/g creatinine)	108.68 $\pm$ 60.19	6.04 $\pm$ 4.58	57.36 $\pm$ 66.82	0.0001

The Pearson correlation test revealed that urine albumin had a direct and significant association with serum creatinine levels in patients with diabetic nephropathy ($r = 0.347$, $p = 0.028$). Furthermore, no relationship was found between serum albumin and other biochemical markers. Assessing serum albumin status by measuring creatinine ($r = -0.305$, $p=0.056$), urea ($r = -0.333$, $p = 0.036$), and HbA1C ($r = -0.376$, $p = 0.017$) was possible in the control group (Table 2).

Table 2. Investigation of the association between the amounts of serum and urine albumin and the biochemical markers of patients with and without diabetic nephropathy

Groups	Chemical parameter (Unit)	Serum albumin		Urine albumin		Total
		Pearson's r	P-value	Pearson's r	P-value	
All patients	Serum albumin (mg/dL)	1	-	-0.490	0.001	80
	Urine albumin (mg albumin/g creatinine)	-0.490	0.001	1	-	80
	HbA1C (%)	0.172	0.126	-0.238	0.034	80
	Urea (mg/dL)	-0.342	0.002	0.527	0.001	80
	Creatinine (gram/mg)	-0.476	0.001	0.597	0.001	80
	Uric acid (mg/dL)	-0.417	0.001	0.467	0.001	80
Patients with diabetic nephropathy	Serum albumin (mg/dL)	1	-	0.107	0.511	40
	Urine albumin (mg albumin/g creatinine)	0.107	0.511	1	-	40
	HbA1C (%)	-0.037	0.819	0.128	0.431	40
	Urea (mg/dL)	0.123	0.451	0.184	0.257	40
	Creatinine (gram/mg)	-0.151	0.353	0.347	0.028	40
	Uric acid (mg/dL)	0.024	0.881	-0.017	0.916	40
Patients without diabetic nephropathy	Serum albumin (mg/dL)	1	-	0.200	0.217	40
	Urine albumin (mg albumin/g creatinine)	0.200	0.217	1	-	40
	HbA1C (%)	-0.376	0.017	-0.041	0.800	40
	Urea (mg/dL)	-0.333	0.036	-0.136	0.404	40
	Creatinine (gram/mg)	-0.305	0.056	0.085	0.601	40
	Uric acid (mg/dL)	-0.037	0.821	0.135	0.408	40

Discussion

In our study, blood albumin levels in diabetic patients with nephropathy were lower than those in the non-nephropathy group; however, nephropathy patients had greater albuminuria and protein excretion than the control group. According to Zhang et al. in 2019, the severity of hypoalbuminemia is substantially related to poor renal outcomes. Patients with the lowest albumin levels compared to the control group had a 7.37-fold increased risk of ESRD. As a result of this study's findings, it is indicated that low serum albumin levels might be helpful in the prognosis of DN. Our findings that patients with lower serum albumin levels are more likely to develop ESRD should notify nephrologists that such patients should be closely monitored and may be treated more extensively and carefully (14). AbuMustafa et al. discovered that serum glucose, urea, creatinine, and cholesterol levels were significantly higher in individuals with type 2 diabetes. Urine albumin and the albumin-to-creatinine ratio (ACR) were 10-13 times higher in diabetic nephropathy patients. In contrast, the glomerular filtration rate (GFR) was significantly reduced in diabetic nephropathy patients (15), which supports the current study's findings.

In our investigation, the nephropathy group had markedly higher serum levels of uric acid, urine albumin, and excreted creatinine than the non-nephropathy group. In addition, when the two groups were compared, it was observed that urine albumin was directly and significantly associated with serum creatinine levels. However, there was no correlation between serum albumin and urine albumin with other measured indicators, including uric acid. Checking serum albumin status by measuring creatinine, urea, and HbA1C was possible and significant in the control and non-diabetic nephropathy groups. Additionally, Kocak et al. found that the serum uric acid levels of diabetic nephropathy patients were considerably greater than those of the non-nephropathy group in a comparable design conducted on 100 patients with type 2 diabetes. According to Kocak et al., there is a significant positive association between microalbuminuria and uric acid (16). Following this conclusion, a study by Latif et al. on 200 patients with type 2 diabetic nephropathy showed a positive association between blood uric acid and creatinine levels and microalbuminuria in type 2 diabetic nephropathy (17). In 2013, Behradmanesh et al. established a positive and significant association between serum and urine uric acid levels (18). A good and substantial link between microalbuminuria and uric acid was identified in a recent study by Warjekar et al. in 2018, which investigated 100 patients with type 2 diabetes as a case group and 100 healthy individuals as a control group. They concluded that hyperuricemia indicates increased glucose intolerance, diabetes, and diabetic nephropathy (19). The difference between the results of the preceding research and ours is that in our study, diabetic patients were classified into two groups with and without nephropathy. In contrast, in the prior studies, patients with and without type 2 diabetes were divided into two groups. The general examination of diabetes patients in our study also revealed a positive and substantial association between urine albumin and serum creatinine, uric acid, and urea, which supports earlier studies.

Khan et al. conducted a study in North India in 2012 that included 42 patients with microalbuminuria and 20 participants with type 2 diabetes who did not have microalbuminuria. HbA1C was considerably greater in patients with microalbuminuria diabetes than in patients without microalbuminuria. In the current study, hemoglobin A1C had a significant negative association with urine albumin in patients with type 2 diabetes, while no relationship was observed between HbA1C and serum or urine albumin in patients with nephropathic diabetes (20).

Regardless of clinical or histological features, low serum albumin content was found to have a notable impact on the prediction of impaired renal function and a poor renal prognosis in T2DM patients. Moreover, total urine albumin and serum creatinine significantly influenced the prediction of renal function in individuals with type 2 diabetic nephropathy because of the observed association.

Conclusion

In a comparative analysis of the two groups participating in this study, it was revealed that high urinary albumin levels in patients with diabetic nephropathy have a direct association with serum creatinine levels, indicating a useful prognostic marker in the evaluation of nephropathy

patients with albuminuria, since the severity of nephropathy is inversely related to serum albumin. However, further research with a larger number of participants is required.

The limitations of this study were the small number of samples and, in some cases, inadequate information. Another drawback of the study was the lack of investigation of GFR and the albumin-to-creatinine ratio, as well as the unknown duration of diabetes and the period of conversion to diabetic nephropathy.

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Ethical Statement

This study was approved by the Ethics Committee of Golestan University of Medical Sciences, Gorgan, Iran (Code: IR.GOUMS.REC.1401.158).

Conflicts of Interest

The authors declare no conflicts of interest.

Author Contributions

Alaa Kazem and Azad Reza Mansurian researched the literature, conceived the study, and were involved in protocol development, gaining ethical approval, and data analysis. Golam Reza Vaghari and Fatemeh Mohammadzadeh wrote the first draft of the manuscript. Seyed Mostafa Mir reviewed and edited the manuscript and approved the final version of the manuscript.

Data Availability Statement

All data supporting the findings of this study are included within the article and its supplementary materials.

Use of Artificial Intelligence

The authors declare that no form of generative artificial intelligence was used in the writing of this manuscript or in the creation of its images, graphics, tables, or corresponding captions.

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