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Research Article

DIABETES MELLITUS TYPE 2 SUBJECTS WITH AND WITHOUT DIABETIC NEPHROPATHY: ANALYSIS OF URINE PODOCALYXIN

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ABSTRACT

Approximately 85% of diabetic cases are Type 2 diabetes mellitus. Diabetes mellitus causes diabetic nephropathy in the kidneys, which can result in kidney failure. As a result of its role in kidney podocyte development, potocalyxin (PDX) is one of the proteins that are expressed in kidney podocytes and that play a role in cancer development. With a purposive probability sampling technique, the sample size was calculated by taking a normal distribution of random samples across the sample size of 35 diabetics with diabetic nephropathy and 35 diabetics without diabetic nephropathy during the study. The results showed that the urinary PDX level in DM subjects with nephropathy were 1.173 ng/mL and DM without nephropathy were 0.167 ng/mL ($p<0.001$), the urine albumin/creatinine ratio (ACR) of DM subjects with nephropathy were 644.74 mg/ g and DM without nephropathy of 10.071 mg/g ($p<0.001$) and the correlation test results of urine PDX and urine ACR in DM subjects with nephropathy ($r=0.520$; $p=0.001$). There was an important difference in urinary PDX levels in diabetic nephropathy compared to diabetic nephropathy, as well as a significant difference in urine ACR levels between diabetic nephropathy and DM with and without diabetic nephropathy, and a significant correlation was found between urinary PDX and urine ACR in diabetic nephropath patients.

Keywords: - Diabetes mellitus, Potocalyxin, Diabetic nephropathy.

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INTRODUCTION

In recent years, the obesity epidemic has resulted in an increase in type 2 diabetes mellitus (T2DM). Micro vascular complications such as retinopathy, nephropathy and neuropathy can occur in individuals with Type 2 DM, as well as macro vascular complications, such as cardiovascular complications resulting from hyperglycaemia and the individual components of the (metabolic) insulin resistance syndrome [1]. It is estimated that diabetic nephropathy causes half of all end-stage kidney failures worldwide [2]. During the course of the disease, a person will develop proteinuria as a result of a decline in their glomerular filtration rate that lasts for a long time, usually between 10 and 20 years. If it is not treated, the result will be morbidity [3]. Symptoms of diabetic nephropathy include kidney failure due to kidney damage caused by diabetes mellitus. The most common cause of death and disability associated with diabetes is nephropathy [3, 4]. CD34 (Cluster of Differentiation 34) is a family of anionic trans membrane sialoglycoproteins produced by podocytes. Glomerular filtration barrier (GFB) is formed by podocytes, which are visceral epithelial cells. In diabetic nephropathy, PDX released from podocytes, resulting in urine PDX (u-PDX), may be useful as an early diagnostic marker for PDX [5].

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The pathological mechanisms of DN are largely determined by podocyte injury. It is known that podositopathy may initially be characterized by podocyte hypertrophy, monomerization of podocytes, a transition from epithelium to mesenchyme (EMT), and release from the glomerular basement membrane as well as apoptosis [6,7]. As DN progresses, podocytes lose their foot processes, podocytes are released through urine, and diaphragmatic filtration slits are damaged, causing proteinuria [8]. Early detection of DN can be achieved through the presence of podocytes and their specific proteins in the urine. There are currently new markers that are being evaluated to detect DN earlier in the disease process when most of the research has been focused on podocyte-specific proteins such as podocalyxin, nephrin, synaptopodin, podocin, mindin, etc. of the podocyte [9]. According to a research [10], podocalyxin plays a new role in morphology of cells. Ectopic expression of podocalyxin significantly enhances microvillus formation in kidney epithelial cells. Further, podocalyxin plays an important role in kidney podocyte foot processes (FP) elongation. There is abundant Podocalyxin in the kidney glomeruli, and it is essential for the development of kidneys. Podocalyxin levels in urine of patients with type 2 diabetes and diabetic nephropathy will be determined and compared.

METHODOLOGY

Patient Participation and Study Design

Cross-sectional observational research design was used for this study.

Clinical Data Collection

Using a non-probability sampling technique, 70 participants were divided into 35 participants with T2DM with DN and 35 participants with T2DM without DN, resulting in 70 participants in total.

Data on pathology

It was inclusive to pregnant women, preeclampsia, lupus nephritis, cancer, hypertension, and coronary heart disease, but excluded pregnant women, preeclampsia, lupus nephritis, cancer, and hypertension. 126 mg/dL of fasting blood glucose levels or HbA1c of 6.5% determined the diagnosis of T2DM participants. Based on urine albumin creatinine ratio (ACR), participants with and without DN were diagnosed with DN by comparing 30 mg/g meaning not diagnosed with diabetic nephropathy to 30 mg/g meaning diagnosed with diabetic nephropathy.

Measurement of Urine Podocalyxin

ELISA (Enzyme-linked Immunosorbent Assay) measured urine podocalyxin levels at wavelength of 450 nm using Assay PharmaGenie® (SBRS1004).

Analyses of statistics

This study was conducted using the SPSS (statistical product and science service) version 23 computer program on Windows. To compare urine podocalyxin levels in subjects of T2DM with and without DN, urine podocalyxin levels in subjects of T2DM with and without DN were compared by using the Mann-Whitney test, along with ACR levels in both groups, and a correlation test was conducted using Spearman's correlation formula. A significant result is defined as a p value of less than 0.05.

RESULTS

A table with an explanation presents the research results. In Table 1, participants' characteristics are listed, such as their gender, age, HbA1c results, and whether they are diagnosed as having diabetes type 2, or as having diabetes type 2, with DN based on ACR and 30 mg/g respectively. T2DM participants with and without DN are compared using urine podocalyxin and ACR levels in Table 2, while T2DM patients with DN are compared using urine podocalyxin and ACR levels.

Table 1: Characteristics of the participants

Characteristics	n	%
Sex		
Male	31	40.3
Female	39	59.7
Ages (years old)		
30 – 40	6	6.8
41 – 50	11	17.2
51 – 60	26	44.3
61 – 70	21	34.3
> 70	6	6.9
HbA1c		
<6.5 %	13	11.3
≥6.5 %	57	88.7

Urine Albumin/Creatinine Ratio		
< 30 mg/g (T2DM with DN)	34	45.7
≥ 30 mg/g (T2DM without DN)	36	54.3

Research participant characteristics are shown in Table 1, with females dominating (59.7%) over males (40.3%). Among the participants, of those between 51 and 60 years of age (44.3%) accounted for the majority of participants. A glycemic control percentage was calculated using HbA1c levels for 57 participants (88.7%) and 13 participants (11.3%). ACR as a biomarker was detected in 36 patients (50.9%). The average urine podocalyxin in patients with nephropathy was 1.173 ng/mL, whereas people without nephropathy, including diabetics, had an average value of 0.167 ng/mL.

Table 2: Diabetic Nephropathy versus Non-diabetic Nephropathy Urine Podocalyxin Levels Comparison

Parameter	Characteristics	Mean	SD	p*
Urine Podocalyxin (ng/mL)	T2DM with DN	1.173	2.088	<0.001
	T2DM without DN	0.167	0.043	

Participants with diabetes nephropathy have an average urine podocalyxin level of 1.173 ng/mL with a standard deviation of 2.088 ng/mL, while those without diabetes nephropathy have an average urinary podocalyxin level of 0.167 ng/mL with a standard deviation of 0.043 ng/mL. As a result of this result, diabetics with nephropathy have a higher average urinary podocalyxin than those without ($p < 0.05$). Participants with diabetic nephropathy produced significantly lower levels of urine podocalyxin than participants without diabetes.

Table 3: An experiment comparing albumin/creatinine ratio levels between diabetics and non-diabetics

Parameter	Characteristics	Mean	SD	p*
Albumin/Creatinine Ratio Levels (mg/g)	T2DM with DN	655.83	1457.22	<0.001
	T2DM without DN	12.082	7.774	

A diabetic nephropathy subject's albumin creatinine ratio averaged 655.83 mg/g with a standard deviation of 1457.22 mg/g, whereas a diabetic nephropathy subject's albumin creatinine ratio averaged 12.082 with a standard deviation of 7.774 (Table 3). Among the results obtained in this study, there was a significant difference between the average albumin creatinine ratio in diabetics with nephropathy and in patients without nephropathy ($p < 0.05$). In participants with and without diabetic nephropathy, the albumin creatinine ratios differed significantly.

Table 4: Test to determine the relationship between albumin/creatinine ratio and urine podocalyxin levels in Diabetic Nephropathy participants

Albumin/Creatinine Ratio		
Urine Podocalyxin	R	0.520
	P	< 0.001
	N	70

In participant with diabetic nephropathy, urine podocalyxin levels were correlated with albumin creatinine ratios in table 4. Among diabetic nephropathy participants, urinary podocalyxin levels correlate with albumin creatinine ratios ($p<0.001$).

DISCUSSION

Participants with and without diabetic nephropathy were assessed for urine podocalyxin levels in this study [11]. The glomerular filtration barrier (GFB) is made up of a main component known as podocalyxin, which plays an important role regulating its permeability [12]. The comparison test for urine podocalyxin between participants with nephropathy and non-nephropathy was carried out in Table 2, and it revealed that urine podocalyxin with nephropathy had a significant difference compared to urine podocalyxin without nephropathy. Among patients with normoalbuminuria, 48.2% increased urine podocalyxin levels, while 64% increased micro albuminuria levels, and 100% increased macro albuminuria levels [13]. According to a study, podocalyxin is found in urine early in diabetic nephropathy, before micro albuminuria develops [14].

The results of a study [15] indicated insufficient expression of PCX in the kidneys and increased PCX excretion through urine, which would be consistent with

the release of PCX protein from the kidney into the urine. PCX has been identified as a biomarker for early kidney damage in patients with diabetic nephropathy, anaphylactic purpuric nephropathy, lupus nephropathy, or IgA nephropathy [16, 17], as well as the development and progression of complications. It is also non-invasive, which means it can be applied to clinical settings in the near future. It included patients with diabetic nephropathy and clinical albuminuria, though previous studies focused on patients with early-stage nephropathy. Several studies have suggested that urinary PCX levels are elevated in nephropathy patients and are significantly correlated with reduced kidney function in individuals with early-stage DN, suggesting the potential clinical utility of PCX levels as a biomarker in the diagnosis of DN.

There are some limitations to this study, including the fact that it used a cross-sectional sampling method that explores only a single event at a time, as well as the small number of respondents enrolled in the study. A large sample size is needed for future prospective studies comparing urine podocalyxin levels to micro albuminuria (MAU) as early detection markers.

CONCLUSIONS

It was concluded that urine podocalyxin levels were different in individuals with and without diabetes type 2, that ACR levels were different in those with diabetic diabetes type 2 with and without diabetes type 2, and that urine podocalyxin levels correlated the most with ACR levels in individuals with diabetes type 2.

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