UDC 616.61 doi: https://doi.org/10.15407/ubj95.05.031

ASSESSMENT OF URINARY PODOCALYXIN AS A BIOMARKER OF EARLY DIAGNOSIS OF HYPERTENSIVE NEPHROPATHY

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Received: 31 August 2023; **Revised:** 28 September 2023; **Accepted:** 27 October 2023

Chronically high blood pressure-related kidney injury is known as hypertensive nephropathy (HN). Podocyte damage in the pathogenesis of this disease can result in the release of the sialoglycoprotein podocalyxin into the urine, so podocalyxin may be useful in the early diagnosis of HN. The purpose of the study was to examine the relationships between urine podocalyxin level and clinical and biochemical parameters in individuals with HN and to assess the diagnostic utility of urinary podocalyxin as an early marker of HN. Participants (114 individuals) were enrolled in this cross-sectional study, including 30 healthy controls and 84 patients with clinically proven chronic hypertension (CH). Biochemical tests were performed on the blood samples. Urinary microalbumin and creatinine levels were measured using immunoturbidimetric and spectrophotometric methods, respectively; urinary podocalyxin level was estimated with ELISA. All CH patients were classified into subgroups according to urine microalbumin/creatinine ratio (UM/CR) and the stage of chronic kidney disease (CKD). The results obtained showed that urinary podocalyxin level was significantly increased in both UM/CR and CKD staging subgroups compared with the healthy control group. A gradual increase in urinary podocalyxin level with CKD stage, especially in IV and V stages, and the higher sensitivity of urinary podocalyxin as compared to UM/CR ratio in early detection of HN was demonstrated. It was concluded that urinary podocalyxin may be an important and highly sensitive marker for early diagnosis of hypertensive nephropathy in patients with chronic hypertension.

K e y w o r d s: hypertensive nephropathy, urine, podocalyxin, microalbumin, creatinine, diagnostic marker.

Hypertensive nephropathy (HN) is the second most common cause of end-stage renal disease (ESRD) after diabetes. The proportion of hypertensive patients who develop end-stage renal disease increases significantly if blood pressure levels are uncontrolled for long periods or if kidney disease is already present. Over 20% of patients with chronic hypertension (CH) have hypertensive nephropathy [1]. Because the early course of HN is often asymptomatic and these patients do not have regular medical evaluations, most patients have early-stage chronic kidney disease at the time of their first medical evaluation. Multiple kidney lesions may have formed before clinical symptoms and routine laboratory results were found to be abnormal. HN can also occur in newly diagnosed hypertensive patients, but the clinical manifestations of HN often appear 10–15 years after the diagnosis of hypertension. Hence, early diagnosis of HN is crucial [2]. Screening of high-risk populations, including those with hypertension, diabetes mellitus, and people over the age of 65, is recommended and includes two laboratory tests: glomerular filtration rate (GFR) and urinary microalbumin as measures of renal function, and urinary microalbumin to creatinine ratio (UM/CR), as a measure of renal impairment [3]. It has been suggested that microalbuminuria may be a marker of early renal dysfunction and a predictor of ESRD and cardiovascular disease, although microalbuminuria is commonly seen in other pathological conditions. Therefore, HN reflects endothelial dysfunction and may be a better predictor of cardiovascular risk than CKD progression [4]. HN is characterized by a combination of pathological changes in vasculature, glomeruli, tubular interstitium, capillary endothelial cells, podocytes, and

immune cells. Over the past two decades, several animal studies have shown that damage to podocytes is important for the pathogenesis of HN [5]. A possible explanation is that increased blood pressure causes podocyte damage through the mechanical effects of glomerular hypertension, hyperfiltration, and glomerular hypertrophy, which results in the detachment of podocytes from the glomerular basement membrane and their excretion through urine [6]. Although human data are limited, several studies have shown that podocyte damage occurs during the early stages of hypertensive renal injury. Podocytes are highly differentiated cells and are critical in maintaining the glomerular filtration barrier. A recently studied mechanism revealed that podocyte extinction and loss led to increased protein leakage and decreased GFR. Therefore, in HN, podocyturia could be a predictor of the clinical outcomes [7]. Podocytes and their specific proteins (such as podocalyxin) are present in the urine when the podocytes are damaged or detached from the glomerular basement membrane. An anionic transmembrane sialoglycoprotein called podocalyxin (PDX) belongs to the CD34 protein family. It is a crucial part of the slit diaphragm structure and is expressed on the apical side of podocyte foot processes. Due to this, urine podocalyxin may serve as a biomarker of podocyte malfunction that can be used to determine the health of the kidney's filtration barrier [8]. Therefore, the measurement of urinary podocalyxin may be a promising tool for the early detection of podocyte injury in HN. Early detection of podocyte damage can enable early treatment and slow the progression of end-stage renal disease. Our study aimed to investigate the association between urinary podocalyxin levels and clinical and laboratory characteristics in patients with HN and to test the diagnostic significance of urinary podocalyxin as an early biomarker for HN.

Material and Methods

Subjects. The Department of Medical and Experimental Biochemistry at the Faculty of Medicine in Skopje conducted this cross-sectional study from March 2016 to May 2017. The research was carried out by the Declaration of Helsinki, and it received approval from the Faculty of Medicine's Ethical Committee in Skopje, North Macedonia (No. 03-5515/8 from 09.12.2015). Participants (84 individuals) with chronic hypertension (CH) (23 with clinically established HN and 61 without clinically proven HN) and 30 healthy controls were included in the current study. From the University Clinic of Nephrology at the Faculty of Medicine in Skopje, patients with HN that had been clinically verified were chosen. The existence of high blood pressure and abnormalities in kidney structure or function (defined by the presence of macroalbuminuria, microalbuminuria, or decreased GFR) present for more than three months met the inclusion criteria for individuals with CH and HN [9]. Diabetes mellitus type 2 and the existence of any other kidney condition met the exclusion criteria. From the Primary Health Care Offices, patients with CH without clinically established HN were sought out as new-onset cases with high blood pressure who had not been seen by nephrologists for the evaluation of renal function, in other words, without clinically proven HN. Each participant in this study gave their informed consent.

According to UM/CR, patients with CH were categorized into three subgroups as follows: 1 – macroalbuminuric subgroup with UM/CR > 300 mg/g (n = 4); 2 – subgroup of people with microalbuminuria, UM/CR 30-300 mg/g (n = 20); 3 – normolbuminuric subgroup (n = 60), UM/CR 30 mg/g.

Five subgroups were created by further categorizing all CH patients according to the stage of CKD: 1 – patient subgroup in stage V with an eGFR of less than 15 ml/min per 1.73 m^2 (n = 1); 2 – patients in stage IV who fall into the eGFR range of 15 to 29 ml/min per 1.73 m^2 (n = 6); 3 – stage III *a* and *b* subgroup, individuals with an eGFR of 30 to 59 ml/min per 1.73 m^2 (n = 30); 4 – stage II patient subgroup, eGFR 60 to 89 ml/min per 1.73 m^2 (n = 38); 5 – subgroup of patients in stage I who fall into the eGFR 90 ml/min per 1.73 m^2 and higher (n = 9).

Both patient classifications were made according to the guidelines of KDIGO – Kidney Disease: Improving Global Outcomes Guidelines [10].

Demographic and clinical data (age, sex, height and weight, duration of illness, comorbidities, laboratory tests, and blood pressure measurements) were collected from all subjects included in this study.

Analysis of urine. As a material, 10 ml of the first voided morning urine samples were collected in a sterile plastic tube and divided: 5 ml for direct estimation of urinary creatinine and microalbumin, and 5 ml after centrifugation for 20 min at 1000 rpm were stored at 80°C. for future measurement of urinary podocalyxin by enzyme-linked immunosorbent assay (ELISA). Urinary microalbumin was

measured using an immunoturbidimetric method, while urinary creatinine was measured using the Jaffe reaction on a ChemWell biochemical analyzer (2910® Awareness Technology, Inc. Palm City, FL, USA). UM/CR was calculated by dividing the urinary microalbumin concentration in milligrams by the urinary creatinine concentration in grams. GFR was estimated by the Cocroft and Gault equation [11].

Frozen urine samples were prepared and evaluated according to the manufacturer's instructions for the urine podocalyx ELISA kit (Exocell Inc., Philadelphia, PA, USA). The method for detecting urinary podocalyxin levels was an indirect competitive ELISA using a rabbit primary antibody against podocalyxin and horseradish peroxidase (HRP)-conjugated anti-rabbit antibody. As an antigen, urinary podocalyxin, competed with podocalyxin antigens immobilized on the bottom of polystyrene microtiter plates with added primary antibodies. Detection of urinary podocalyxin-restricted primary antibodies was achieved using anti-rabbit HRP antibodies. Several washing steps removed unbound antibodies, and then the chromogenic substrate was added, resulting in color development. The intensity of the developed color was inversely proportional to the concentration of podocalyxin in the urine sample and was measured photometrically at 450 nm. Urine podocalyxin levels were estimated from a standard curve determined using commercial standards provided by the ELISA kit. Urinary podocalyxin levels were expressed as ng/ml.

Blood analysis. From all subjects, 5 ml venous blood samples were aseptically collected into a standard tube and allowed to clot for 10–15 min. The serum was separated by centrifugation at 3000 rpm for 10 min. Isolated serum was measured for blood glucose, low-density lipoprotein (LDL), high-density lipoprotein (HDL), total cholesterol, triglycerides, blood urea, serum creatinine, total protein, and albumin using a ChemWell biochemical analyzer (2910® Awareness Technology, Inc. Palm City, FL, USA).

Statistics. Statistical analysis was performed using IBM SPSS Statistics for Windows version XX (IBM Corp., Armonk, N.Y., USA) and MedCalc for Windows version 15.0 (MedCalc Software, Ostend, Belgium). Numerical data are presented as the median and interquartile range (IQR) (25^{th} to 75^{th} percentile), as all data identified by the Kolmogorov-Smirnov test are non-normally distributed. We used the Kruskal-Wallis test to compare differences between more than two groups for clinical and laboratory data and the Mann-Whitney U test to compare differences between two groups for clinical and laboratory data. The Mann-Whitney U test was used as a post-hoc test for the Kruskal-Wallis test to identify significantly different responses. Bonferroni corrections were used when multiple comparisons were made with the same data set. The receiver operating characteristic (ROC) curve analysis was performed to determine the optimal cut-off values for urinary podocalyxin and UM/CR and to measure their diagnostic accuracy in patients with HN. P values ≤ 0.05 were considered statistically significant.

Results

Clinical and biochemical characteristics of study subgroups. Statistical analysis showed a significant difference in age, serum creatinine, body mass index (BMI), systolic blood pressure (SBP), diastolic blood pressure (DBP), blood glucose, LDL, total cholesterol, triglycerides, blood urea, UM/CR, total protein, albumin, and urinary podocalyxin of UM/CR divided between subgroups of subjects. There was a significant difference in subgroups of patients divided by CKD stage according to age, disease duration, serum creatinine, BMI, SBP, DBP, blood glucose level, HDL, total cholesterol, triglycerides, blood urea, UM/CR, total proteins, albumin, and urinary podocalyxin. Tables 1 and 2 show the results of tests of differences for clinical and biochemical data in patients stratified by UM/CR and stage of CKD and healthy controls.

Urinary podocalyxin levels in study subgroups. In subgroups of subjects divided according to UM/CR, the urinary podocalyxin level was significantly elevated compared to healthy controls ($P < 0.05$), Fig. 1. The urinary podocalyxin level was also significantly elevated in subgroups of patients with CH divided according to CKD stage compared to healthy controls ($P < 0.05$), Fig. 2.

Diagnostic performance of urinary podocalyxin and UM/CR in patients with CH. To test the diagnostic performance of urinary podocalyxin and UM/CR and detect the optimal cut-off value for urinary podocalyxin and UM/CR, ROC analysis was performed. To determine the best cut-off, we maximize both Se and Sp with their summation (Se + Sp). At this point, Youden's index (Se + Sp – 1) is also maximum, so the optimal cut-off was calculated from the maximum Youden index (sensitivity + specificity – 1) [12]. The total accuracy of urinary

ISSN 2409-4943. Ukr. Biochem. J., 2023, Vol. 95, N 5

Table 1. Clinical and biochemical characteristics of chronic hypertensive patients divided according to UM/CR and healthy controls

Parameters	Macroalbuminuric patients, *n* = 4	Microalbuminuric patients, *n* = 20	Normoalbuminuric patients, *n* = 60	Healthy controls, *n* = 30	Kruskal-Wallis *P*-value
Age (years)	64.5 (59.5-72.5)	57.5 (46-60.5)	59.5 (54-62)	48 (41-55)	<0.001
Duration of disease (years)	8.5 (5-10)	5 (1-5)	5 (2-5)	/	0.570
BMI (kg/m^2)	32.9 (27.5-35.5)	27.4 (26.2-30.2)	28.5 (26.5-31.8)	25.7(23.1-27.8)	0.001
Blood glucose (mmol/l)	6.06 (4.9-6.56)	5.87 (4.7-8.2)	5.7 (4.6-6.9)	3.9 (3.61-4.87)	<0.001
UM/CR (mg/g)	686.7 (525.6-715.2)	76.9 (52.4-144.6)	11.9 (7.35-18.7)	11 (8.3-16.1)	<0.05
SBP (mm/Hg)	155 (145-165)	147.5 (140-155)	140 (140-150)	120 (110-130)	<0.001
DBP (mm/Hg)	90 (90-95)	90 (90-100)	90 (90-100)	80 (70-90)	<0.001
Total cholesterol (mmol/l)	6.06 (4.83-7.58)	4.8 (3.64-5.17)	4.42 (3.46-4.96)	3.35 (2.59-4.11)	<0.001
Triglycerides (mmol/l)	2.24 (1.33-4.58)	2.18 (1.55-3.68)	1.36 (0.84-2.22)	1.22 (0.66-1.64)	<0.001
HDL (mmol/l)	1.27 (0.92-1.7)	1.24 (0.93-1.3)	1.25 (0.92-1.56)	1.22 (0.9-1.56)	0.938
LDL (mmol/l)	3.36 (2.89-4.21)	2.51 (1.7-2.76)	2.33 (1.5-3.0)	1.73 (1.0-2.09)	0.005
Total proteins (g/l)	68 (61.5-74.5)	70 (64.5-72)	65.5 (57-74)	74.5 (70-78)	0.001
Albumin (g/l)	39 (36.5-40)	40 (38.5-44.5)	39 (35.5-44)	47 (45-48)	<0.001
Blood urea (mmol/l)	10.25 (6.03-14.8)	6.12 (5.13-10.0)	6.44 (5.47-8.61)	4.39 (3.47-4.97)	<0.001
Serum creatinine (μmol/l)	171.5 (84.1-243.8)	84.1 (68.6-97.2)	76.7 (69-91.5)	76.8 (65.3-84.1)	0.001
eGFR (ml/min per 1.73 m^2)	35.5 (16.9-58.5)	58.4 (40.9-72.5)	63.8 (54.9-73.1)	91.14 (86.6-95.5)	<0.001
Urinary podocalyxin (ng/ml)	61.2 (54.05-111.2)	54.8 (33.5-72.7)	45 (32.8-60.7)	24.3 (14.9-38.5)	<0.001

Note. Results are presented as median and interquartile range (IQR). Abbreviations: BMI – body mass index, UM/CR – urinary microalbumin to creatinine ratio, SBP – systolic blood pressure, DBP – diastolic blood pressure, HDL – high-density lipoproteins, LDL – low-density lipoproteins, eGFR – estimated glomerular filtration rate

Table 2. Clinical and biochemical characteristics of chronic hypertensive patients divided according to CKD stage and healthy controls

Parameters	I stage, *n* = 9	II stage, *n* = 38	III stage, *n* = 30	IV stage, *n* = 6	V stage, *n* = 1	Healthy controls, *n* = 30	Kruskal-Wallis *P*-value
Age (years)	54 (39-59.5)	59 (53-61)	60 (58-64)	64.5 (59-78)	56	48 (41-55)	<0.001
Duration of disease (years)	4 (1-5)	4.5 (2-5)	5 (2-5)	10 (7-20)	20	/	0.036
BMI (kg/m^2)	30.2 (28.8-37.4)	29.1 (27-32.6)	27.5 (24.8-29.4)	25.5 (23.7-26.9)	26.8	25.7 (23.1-27.8)	<0.001
Blood glucose (mmol/l)	6.7 (4.4-8.3)	5.8 (4.5-6.9)	5.4 (4.73-7)	6.1 (5.7-6.9)	7.6	3.9 (3.61-4.87)	0.002
UM/CR (mg/g)	27.4 (15.4-67.5)	14.6 (7.7-22.6)	17.25 (8.9-30.4)	135.3 (23.2-365.7)	85.8	11 (8.3-16.1)	0.003
SBP (mm/Hg)	140 (135-147.5)	140 (140-150)	140 (140-160)	150 (145-160)	150	120 (110-130)	<0.001
DBP (mm/Hg)	90 (85-97.5)	90 (90-100)	90 (90-100)	95 (90-100)	90	80 (70-90)	<0.001
Total cholesterol (mmol/l)	4.9 (3.9-6.6)	4.4 (3.4-4.9)	4.8 (4-5.29)	4.7 (3.5-6.9)	4.7	3.35 (2.59-4.11)	0.002
Triglycerides (mmol/l)	3.58 (1.54-6.6)	1.47 (0.9-2.1)	1.23 (0.93-2.89)	2.1 (0.74-4.71)	4.6	1.22 (0.66-1.64)	<0.001
HDL (mmol/l)	1.15 (0.84-1.28)	1.13 (0.8-1.5)	1.27 (1.0-1.5)	1.73 (1.56-1.85)	1.3	1.22 (0.9-1.56)	0.022
LDL (mmol/l)	2.17 (1.61-2.72)	2.27 (1.44-2.84)	2.55 (2.13-3.07)	1.8 (1.2-3.8)	1.3	1.73 (1.0-2.09)	0.086
Total proteins (g/l)	70 (58-78)	65 (56-73)	67 (61-73)	75.5 (70-80)	70	74.5 (70-78)	<0.001
Albumin (g/l)	40 (34.5-44)	38 (35-41)	40 (38-45)	43.5 (40-48)	40	47 (45-48)	<0.001
Blood urea (mmol/)	7.09 (5.22-8.6)	6.06 (5.1-7.6)	6.56 (5.85-8.77)	12.5 (9.41-16.6)	16.6	4.39 (3.47-4.97)	<0.001
Serum creatinine (μmol/l)	62.1 (51.5-80.5)	71.8 (67.8-83.3)	87 (73.5-103)	247.4 (237-260)	467	76.8 (65.3-84.1)	<0.001
eGFR (ml/min per 1.73 m^2)	79.2 (93.05-108.5)	69.7 (64.2-73.4)	53.5 (48.5-55.7)	16.9 (16.02-18.12)	12.4	91.14 (86.6-95.5)	<0.001
Urinary podocalyxin (ng/ml)	64.4 (48.1-89.7)	45 (28.4-61.2)	49.8(38.7-61.2)	51.7 (37.2-142.4)	70.4	24.3 (14.9-38.5)	<0.001

Note. Results are presented as median and interquartile range (IQR). Abbreviations: BMI – body mass index, UM/CR – urinary microalbumin to creatinine ratio, SBP – systolic blood pressure, DBP – diastolic blood pressure, HDL – high-density lipoproteins, LDL – low-density lipoproteins, eGFR – estimated glomerular filtration rate

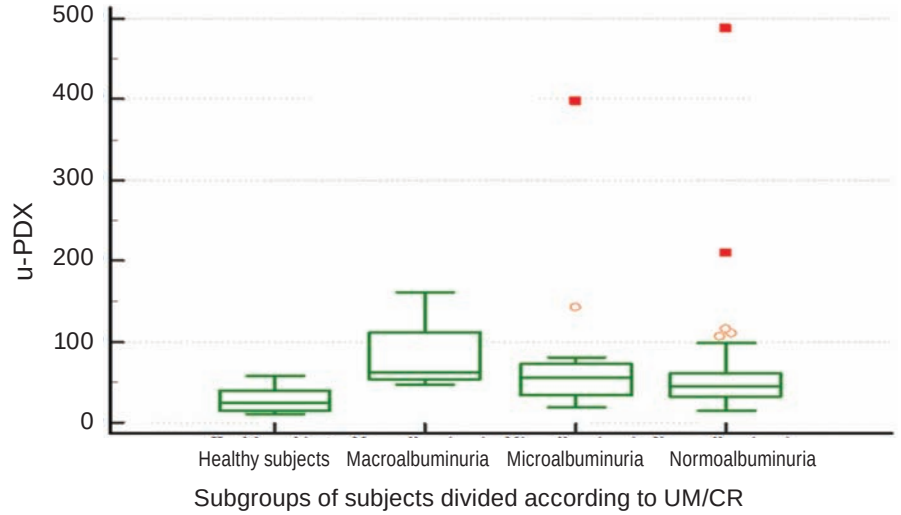

Fig. 1. Comparison of urinary podocalyxin (u-PDX) levels among subgroups of patients with CH divided according to UM/CR and healthy subjects

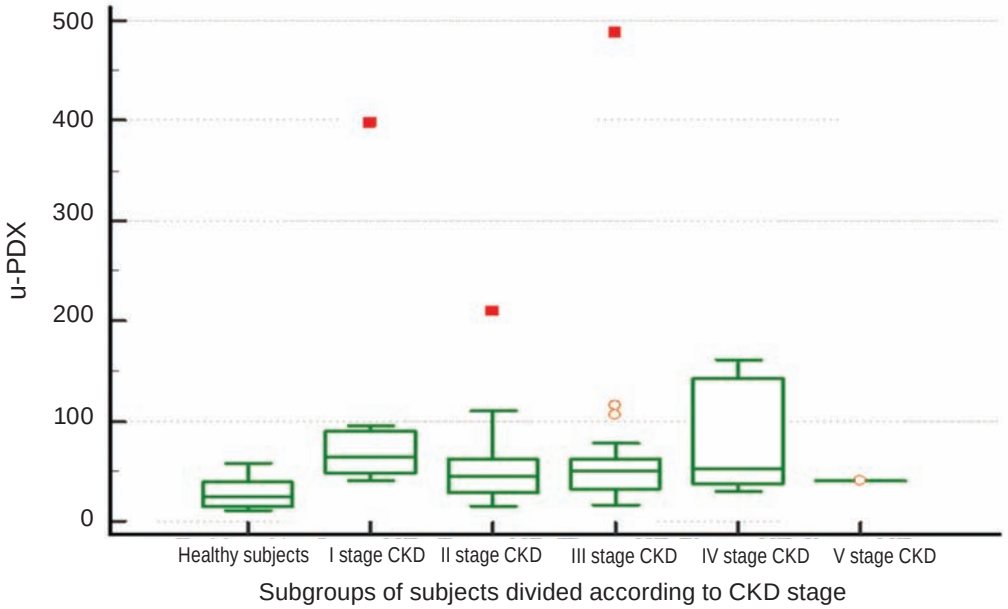

Fig. 2. Comparison of urinary podocalyxin levels among subgroups of patients with CH divided according to CKD stage

podocalyxin was 66.6%, while UM/CR's total accuracy was 57.8% in early diagnosis of HN. Results are presented in Table 3.

Percentage of subjects with elevated urinary podocalyxin in study subgroups. In subgroups of patients divided according to UM/CR, urinary podocalyxin levels were higher than the cut-off value (>58.9 ng/ml) in 25% of patients with normoalbuminuria, in 75% of patients with microalbuminuria and 90% of patients with macroalbuminuria (Fig. 4).

In subgroups of patients divided according to CKD stage, urinary podocalyxin levels were higher than the cut-off value in patients in CKD stages V, in 85% of IV stages, in 20% of patients in CKD stage III, 25% of patients in CKD stage II and 70% of patients in CKD stage I (Fig. 5).

Discussion

Patients with CKD up to stage 3, and most cases of stage 4 CKD, are usually asymptomatic,

Table 3. ROC analysis diagnostic performance data of urinary podocalyxin and UM/CR in patients with HN

Diagnostic performance data	Urinary podocalyxin	UM/CR
The area under the ROC curve (AUC)	0.586	0.626
95% Confidence interval (95% CI)	0.474 to 0.693	0.531 to 0.715
Significance level *P* (Area = 0.5)	0.227	0.0148
Youden index J	0.2431	0.3098
Cut-off value	>58.9 ng/ml	>30.0 mg/g
Sensitivity	52.1%	44.8%
Specificity	72.1%	86.1%
NPV negative predictive value	80%	87.5%
PPV positive predictive value	41.3%	41.8%
Diagnostic effectiveness (accuracy)	66.65%	57.8%

Note. NPV – negative predictive value, PPV – positive predictive value, UM/CR – urinary microalbumin to creatinine ratio, HN – hypertensive nephropathy

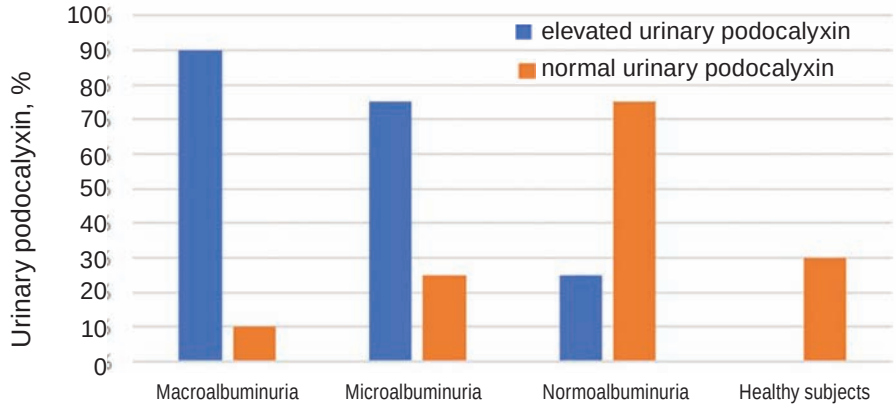

Fig. 3. Elevated urinary podocalyxin in subgroups of patients divided according to UM/CR

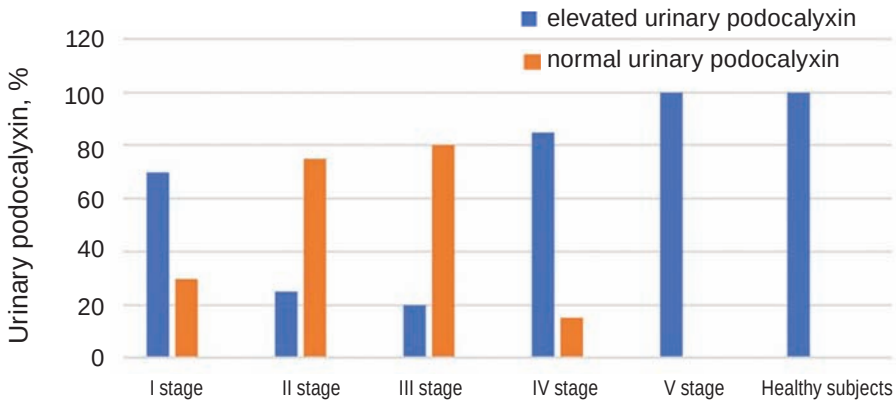

Fig. 4. Elevated urinary podocalyxin in subgroups of patients divided according to CKD stage

which is why CKD is often referred to as the "silent killer". Early detection of CKD in asymptomatic individuals can be accomplished with simple tests such as eGFR and UM/CR, and the necessary measures should be taken to reduce progression to ESRD [13]. Microalbuminuria in CH patients has been described as an early marker of renal injury and a predictor of ESRD and cardiovascular disease with an incidence of approximately 50% [4]. However, some patients with CH may have decreased eGFR and progress to ESRD without significant microalbuminuria or macroalbuminuria, whereas some patients with normal albuminuria or microalbuminuria have progressive renal pathological changes suggest microalbuminuria [14]. In animal models of hypertension, damage to leg cells has been observed with the onset of kidney disease [15, 16]. In contrast, human data on urinary foot cell damage and loss in patients with CH are scarce. A recent study showed that podocyturia occurs in the early stages of hypertensive renal injury and may be a sensitive predictor of HN [5, 6]. In our study, urinary podocalyxin concentrations were estimated in hypertensive patients with and without clinically proven HN to investigate the role of urinary podocalyxin in the early diagnosis of HN. The results of our study showed significant differences in most of the clinical and biochemical parameters (shown in Tables 1 and 2). A significant difference was found regarding urinary podocalyxin between the CH groups divided by CKD stage and the hypertensive patient groups divided by UM/CR. In addition, urinary podocalyxin concentrations were significantly increased in the UM/CR subgroups and the CKD staging subgroups compared with healthy controls ($P < 0.05$). Our results show that urine podocalyxin levels gradually increase with the stage of chronic kidney disease and kidney damage, making it an early marker of HN. The severity of kidney damage is often related to the extent and duration of high blood pressure. Microalbuminuria had a lower sensitivity and total diagnostic accuracy for predicting HN than urinary podocalyxin, according to ROC analysis. For UM/CR 30 mg/g detection, the reported sensitivity, specificity, and positive/negative predictive values were 44.8, 86.1, 87.5, and 41.5%, respectively. The urinary podocalyxin sensitivity, specificity, and positive/negative predictive values were 52.1, 72.1, 80.0, and 41.3%, respectively. The total diagnostic accuracy was higher for urinary podocalyxin than UM/CR and the values were 66.6 and 57.8%, respectively.

We failed to find data regarding the sensitivity and specificity of urine podocalyxin in HN patients in the literature, as well as data on levels of urinary podocalyxin in patients with hypertensive nephropathy. The early data are encouraging, despite the fact that the diagnostic value of urinary podocalyxin for chronic renal disease is yet not fully understood. In glomerular diseases, the level of urinary podocalyxin and the number of urinary podocytes were associated with the proportion of segmental sclerosis. The expression of the kidney function biomarkers serum creatinine, eGFR, and albuminuria was linked with urinary PDX mRNA [17]. We determined that 25% of patients with normoalbuminuria and 70% of patients in stage I CKD have higher urine podocalyxin levels. These findings suggest that in the early stages of CH-related CKD, urinary podocalyxin first appears in the urine preceding microalbumin. Due to the relatively small sample size of the population we analyzed and the cross-sectional nature of our study, additional research and follow-up are required to support our findings. Urinary podocalyxin could be used in common laboratory practice as an early diagnostic marker of HN in patients with CH if additional studies confirm our findings. Our major conclusions include a high percentage of normoalbuminuric patients with CH, and patients in CKD stage I, with elevated urinary podocalyxin levels, a gradual increase in urinary podocalyxin levels with CKD stage, especially in IV and V stage, and higher sensitivity of urinary podocalyxin in early detection of HN compared to UM/CR. We can conclude that urinary podocalyxin may be an important and highly sensitive marker for early diagnosis of HN in CH patients.

Conflict of interest. Authors have completed the Unified Conflicts of Interest form at http://ukr-biochemjournal.org/wp-content/uploads/2018/12/coi_disclosure.pdf and declare no conflict of interest.

ОЦІНКА ПОДОКАЛІКСИНУ В СЕЧІ ЯК БІОМАРКЕРА ДЛЯ РАННЬОЇ ДІАГНОСТИКИ ГІПЕРТОНІЧНОЇ НЕФРОПАТІЇ

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Хронічне ураження нирок, пов'язане з високим артеріальним тиском відомо як гіпертонічна нефропатія (ГН). Пошкодження подоцитів в патогенезі цього захворювання призводить до виділення в сечу сіалоглікопротеїну подокаліксину, тому подокаліксин може бути важливим для ранньої діагностики ГН. Метою дослідження було вивчити взаємозв'язок між рівнем подокаліксину в сечі та клінічними і біохімічними параметрами в осіб із ГН, а також оцінити діагностичну корисність подокаліксину в сечі як раннього маркера ГН. Серед 114 учасників цього перехресного дослідження, було 30 здорових осіб контрольної групи та 84 пацієнтів із клінічно підтвердженою хронічною артеріальною гіпертензією (ХГ). У всіх учасників було проведено біохімічне дослідження крові. Рівень мікроальбуміну та креатиніну в сечі вимірювали за допомогою імунотурбідиметричного та спектрофотометричного методів відповідно; рівень подокаліксину в сечі оцінювали за допомогою ELISA. Пацієнтів із ХГ було розподілено на підгрупи за співвідношенням мікроальбумін/креатинін сечі (UM/CR) та стадією хронічної хвороби нирок (ХХН). Отримані результати показали, що рівень подокаліксину в сечі був суттєво підвищений в обох досліджуваних підгрупах UM/CR та ХХН порівняно з контрольною групою. Продемонстровано поступове підвищення рівня подокаліксину в сечі зі зростанням стадії ХХН, особливо в IV та V стадіях, а також більш високу чутливість подокаліксину в сечі порівняно зі співвідношенням UM/CR при ранньому виявленні ГН. Зроблено висновок, що подокаліксин у сечі може бути важливим і високочутливим маркером для ранньої діагностики гіпертонічної нефропатії у пацієнтів із хронічною гіпертензією.

Ключові слова: гіпертонічна нефропатія, сеча, подокаліксин, мікроальбумін, креатинін, діагностичний маркер.

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