IOSR Journal of Dental and Medical Sciences (IOSR-JDMS)
e-ISSN: 2279-0853, p-ISSN: 2279-0861.Volume 25, Issue 4 Ser.1 (April 2026), PP 81-88
www.iosrjournals.org

Diagnostic Significance of Urinary Podocalyxin in Patients with Diabetic Nephropathy

Dr. Taslima Akter

Abstract
Background: *Diabetic nephropathy is one of the primary causes of end-stage renal disease in the world, and renal disease diagnosis is a clinical issue. The traditional biomarkers, like microalbuminuria, reveal the damage to the kidney at a very late stage. This study aimed to assess the clinical importance of urinary podocalyxin in diabetic nephropathy at different stages of albuminuria.*
Methods: *This cross-sectional study was conducted at Bangladesh Medical University from March 2024 to February 2025 on 50 diabetic patients and subdivided them into Group I (microalbuminuria, n=25) and Group II (normoalbuminuria, n=25). ELISA was used to measure urinary podocalyxin; standard tests were used to measure HbA1c, urinary microalbumin, and serum creatinine. The ROC curve analysis was used to examine the diagnostic performance. Data were entered and analyzed using SPSS version 26.*
Results: *Group I had a very high level of urinary podocalyxin than Group II because of (7.89 ±1.13 vs. 5.11±0.99 ng/mL, p<0.001). The difference in HbA1c, serum creatinine, and eGFR was also significantly different (p<0.001). Microalbuminuria and normoalbuminuria had AUCs of 0.962 and 0.846, respectively (cut-off 7.21 ng/mL and 3.04 ng/mL respectively; sensitivity 79% and specificity 83.1%) as indicated by ROC analysis. There were significant inverse correlations between uPCX and eGFR, and positive correlations between uPCX and HbA1c and urinary microalbumin.*
Conclusion: *Urinary podocalyxin is highly upregulated in diabetic nephropathy and has an excellent diagnostic accuracy in the detection of glomerular injury in microalbuminuric and normoalbuminuric patients. It can be used as an effective, non-invasive, early biomarker of diabetic nephropathy, which supplements the traditional screening instruments.*
Keywords: *Urinary podocalyxin, Diabetic nephropathy, Albuminuria*

I. INTRODUCTION

DM is a metabolic disease that is highly prevalent all over the world and a major cause of chronic kidney disease (CKD). Diabetic nephropathy (DN) is one of the gravest microvascular complications of diabetes that occurs in about 3040% of patients with type 2 diabetes mellitus and is the most prevalent cause of end-stage renal disease (ESRD) worldwide [1]. The worldwide prevalence of diabetic nephropathy is increasing along with the increasing number of patients acquiring diabetes, and developing countries such as Bangladesh have a disproportionate burden [2]. The pathological changes of diabetic nephropathy include progressive damage to the glomerulus, namely, podocyte loss, thickening of the glomerular basement membrane, mesangial proliferation, and tubular atrophy [3]. The outermost glomerular filtration barrier is made up of terminally differentiated, highly specialized visceral epithelial cells called podocytes. Their integrity is vital to preventing proteinuria and glomerular renal filtration. Nowadays, podocyte injury and detachment are seen as the key events of diabetic nephropathy initiation and progression [4]. The podocalyxin (PODXL) is a cell surface glycoprotein that is highly sialylated and exhibits a high expression concentration on the luminal surface of podocyte foot processes. It has a crucial role of preserving the electronegativity of the glomerular filtration barrier and the structure of the podocyte foot processes [5]. Urinary podocalyxin (uPCX) is shed into the urinary space under conditions of podocyte stress or injury, and thus it offers great potential as a non-invasive biomarker of glomerular injury and podocyte loss [6]. The most frequently used biomarkers of diabetic nephropathy that are currently available (urinary microalbumin and estimated glomerular filtration rate (eGFR)) have serious limitations. The onset of microalbuminuria is a relatively late disease event, and is not an effective predictor of early or normoalbuminuric diabetic nephropathy, when preclinical levels of histological injury are evident without proteinuria in the urine [7]. EGFR and serum creatinine are not sensitive measures of early renal injury as well. It is thus a pressing requirement to find early, sensitive, and specific biomarkers that can be used to identify podocyte damage before the development of an open proteinuria. Several studies have shown high levels of urinary podocalyxin in diabetic nephropathy patients relative to the healthy controls and normoalbuminuric diabetic patients [8]. It was found that urinary podocalyxin is negatively correlated with eGFR and positively correlated with urinary albumin excretion, which indicates its possible use as a sensitive early sign of glomerular injury [9]. Besides, it is suggested that uPCX can be a more reliable measure of podocyte damage compared to albuminuria, and may address the earlier detection of

nephropathic change [10]. Nevertheless, urinary podocalyxin has yet to be implemented into the clinical routine, and there has been limited evidence on the diagnostic performance of urinary podocalyxin in the various stages of diabetic nephropathy, especially in South Asian populations. This study was hence conducted to determine the diagnostic value of urinary podocalyxin in patients with diabetic nephropathy, both in micro- and normoalbuminuric patients, in the state of micro- and normoalbuminuric nephropathy by the use of receiver operating characteristic (ROC).

II. METHODS

This cross-sectional analytical study was conducted from March 2024 to February 2025, spanning a period of twelve months, at the Departments of Laboratory Medicine, Endocrinology, and Nephrology of Bangladesh Medical University, Dhaka, Bangladesh. A total of 50 diagnosed patients with diabetes mellitus aged 18 years or older attending both inpatient and outpatient services were enrolled via non-randomized consecutive sampling. Participants were categorized into two groups: Group I (n=25) comprising diabetic patients with microalbuminuria (urinary microalbumin 30-300 mg/g creatinine), and Group II (n=25) comprising diabetic patients with normoalbuminuria (<30 mg/g creatinine). Patients were excluded if they had chronic kidney disease of non-diabetic etiology, urinary tract infection, uncontrolled hypertension, pregnancy, history of nephrotoxic drug use, or established cardiovascular disease, including coronary artery disease, stroke, or peripheral vascular disease. Following institutional ethical approval and written informed consent, demographic and clinical data were recorded using a semi-structured case record form. Anthropometric parameters (height, weight, BMI) and blood pressure were measured. From each participant, 10 mL of random urine and 4 mL of venous blood were collected under aseptic conditions. Urine samples were centrifuged and stored at −20°C. Key variables included urinary podocalyxin (ELISA, sandwich method), urinary microalbumin (immunoturbidometric method), HbA1c (immunoturbidometric method), serum creatinine (spectrophotometry), and estimated glomerular filtration rate (eGFR, calculated via MDRD equation). Data were analyzed using SPSS version 26. Quantitative variables were expressed as mean ± standard deviation and compared using the unpaired t-test. Qualitative variables were compared using the Chi-square test. Diagnostic performance of urinary podocalyxin was assessed by sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), accuracy, and area under the receiver operating characteristic (ROC) curve (AUC). A p-value <0.05 was considered statistically significant.

III. RESULTS

The demographic and anthropometric profiles of both groups of the study are summarized in Table 1. Group I (51.44±10.97 years) and Group II (51.36±11.39 years; p=0.816) had a similar mean age. There were no considerable variations in height or weight. Nevertheless, BMI in the microalbuminuric cohort was much more dominant (25.93 ± 4.61 vs. 23.83 ± 3.15 kg/m 2, p=0.032), which indicates the role of metabolism in nephropathy development.

Table 1: Demographic and Anthropometric Profiling of the study population (N = 50)

Variables	Group I (n = 25)	Group II (n = 25)	p-value
Age (Years)	-	-	-
18-30	0 (0%)	1 (4%)	-
31-40	3 (12%)	3 (12%)	-
41-50	9 (36%)	10 (40%)	-
51-60	8 (32%)	8 (32%)	-
61-70	5 (20%)	3 (12%)	-
Age (Mean ± SD)	51.44 ± 10.97	51.36 ± 11.39	0.816
Sex	-	-	-
Male	8 (32.0%)	14 (56.0%)	-
Female	17 (68.0%)	11 (44.0%)	0.154
Height (feet) (Mean ± SD)	5.30 ± 0.24	5.34 ± 0.19	0.203
Weight (kg) (Mean ± SD)	66.40 ± 12.75	62.24 ± 8.76	0.111
BMI (kg/m²) (Mean ± SD)	25.93 ± 4.61	23.83 ± 3.15	0.032

Table 2 gives a comparison of biochemical parameters. Group I had significantly higher HB A1c (8.60 ± 0.99% vs. 5.97 ± 0.38%), serum creatinine (2.17 ± 0.43 vs. 1.89 ± 0.33 ml/dl), urinary microalbumin (94.25 ± 18.51 vs. 19.18 ± 4.78mg/g), and urinary podocalyxin (7.89 += 1.13 vs. 5.11 ± 0.99).

Table 2: Comparison of biochemical parameters among the study subjects (N = 50)

Variables	Group I (n = 25) Mean ± SD	Group II (n = 25) Mean ± SD	p-value
HbA1c (%)	8.60 ± 0.99	5.97 ± 0.38	0.001
Serum Creatinine (mg/dl)	2.17 ± 0.43	1.89 ± 0.33	<0.001
eGFR (ml/min/m²)	73.58 ± 10.32	96.34 ± 5.05	0.001

Urinary Microalbumin (mg/g)	94.25 ± 18.51	19.18 ± 4.78	<0.001
Urinary Podocalyxin (ng/ml)	7.89 ± 1.13	5.11 ± 0.99	<0.001

In Table 3, the direct comparison of urinary podocalyxin concentrations in groups is obtained. The percentage composition of relative podocalyxin was 60.72% in Group I, and 39.28% in Group II with a highly significant difference ($p<0.001$), which validates that podocalyxin rise is associated with more severe glomerular damage in the nephropathy of microalbuminuric diabetic.

Table 3: Comparison of urinary podocalyxin concentration between groups (N = 50)

Parameter	Group I (n = 25)	Group II (n = 25)	p-value
Urinary Podocalyxin (ng/ml), Mean ± SD	7.89 ± 1.13	5.11 ± 0.99	<0.001*
Relative proportion (%)	60.72%	39.28%	

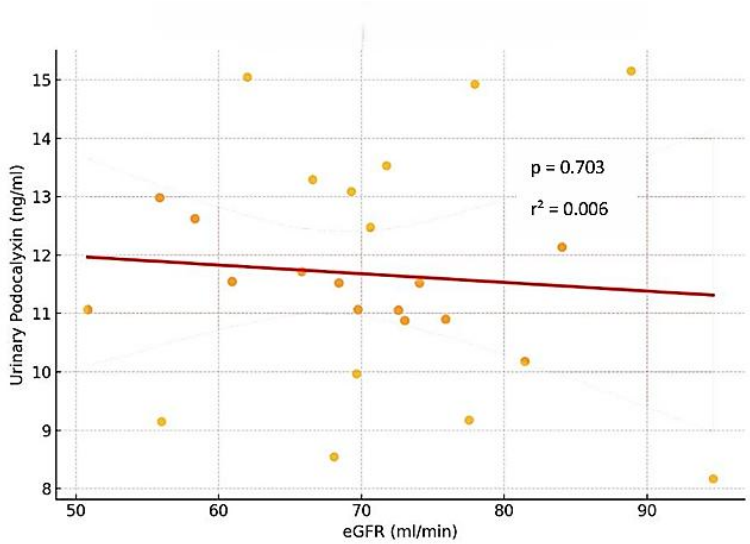

Figure 1: Correlation of eGFR with urinary podocalyxin in microalbuminuria

Figure 1 illustrates a meaningful negative relationship between eGFR and urinary podocalyxin in those with microalbuminuria, indicating that the greater the concentration of podocalyxin, the greater the deterioration of glomerular filtration.

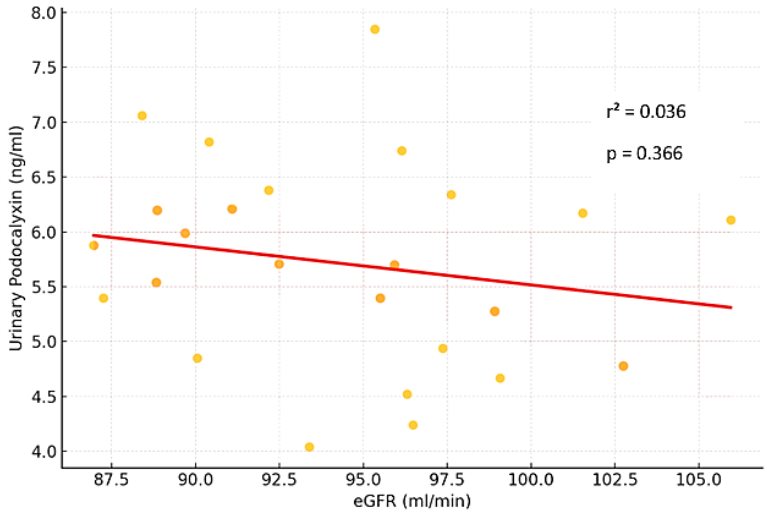

Figure 2: Correlation of eGFR with urinary podocalyxin in normoalbuminuria

The relationship between eGFR and urinary podocalyxin in normoalbuminuric patients is shown in Figure 2. Even where it is not overtly proteinuric, it is found to have an inverse relationship, and this supports the usefulness of podocalyxin as a subclinical indicator of early glomerular damage before the development of albuminuria.

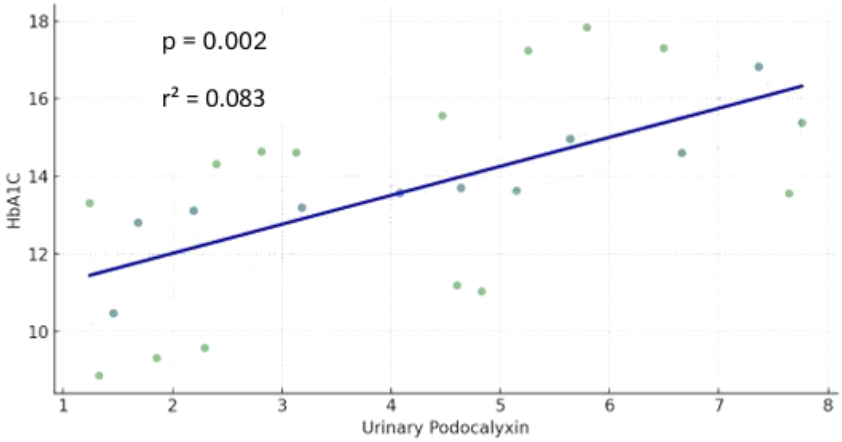

Figure 3: Correlation of HbA1C with urinary podocalyxin in microalbuminuria

Figure 3 demonstrates that the relationship between HbA1c and urinary podocalyxin is positive in the microalbuminuric group, which further proves that worse glycemic control is directly linked to increased podocyte shedding, and hyperglycemia is a core cause of glomerular nephropathy injuries in diabetes.

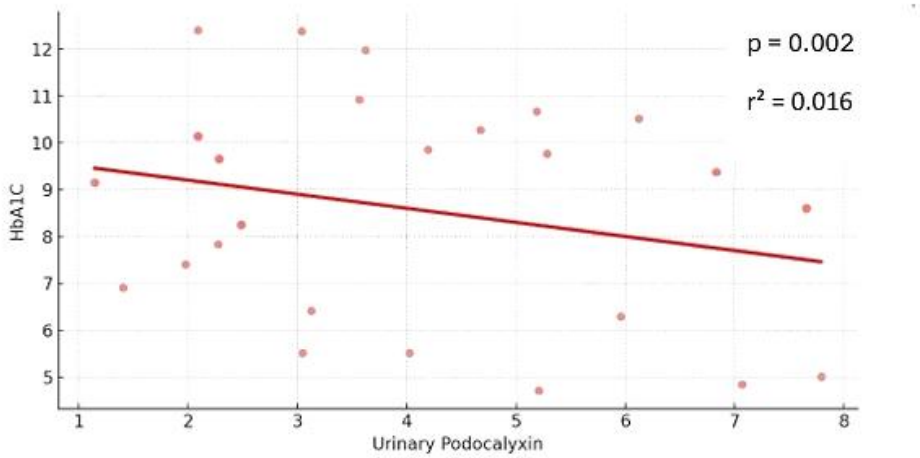

Figure 4: Correlation of HbA1C with urinary podocalyxin in normoalbuminuria

Figure 4 shows that there is a correlation between HbA1c and urinary podocalyxin in normoalbuminuric patients with diabetes. There is a positive correlation, which suggests that regardless of the stage of the disease, the increase in HbA1c values is associated with the growth of podocyte damage measured by the levels of urinary podocalyxin.

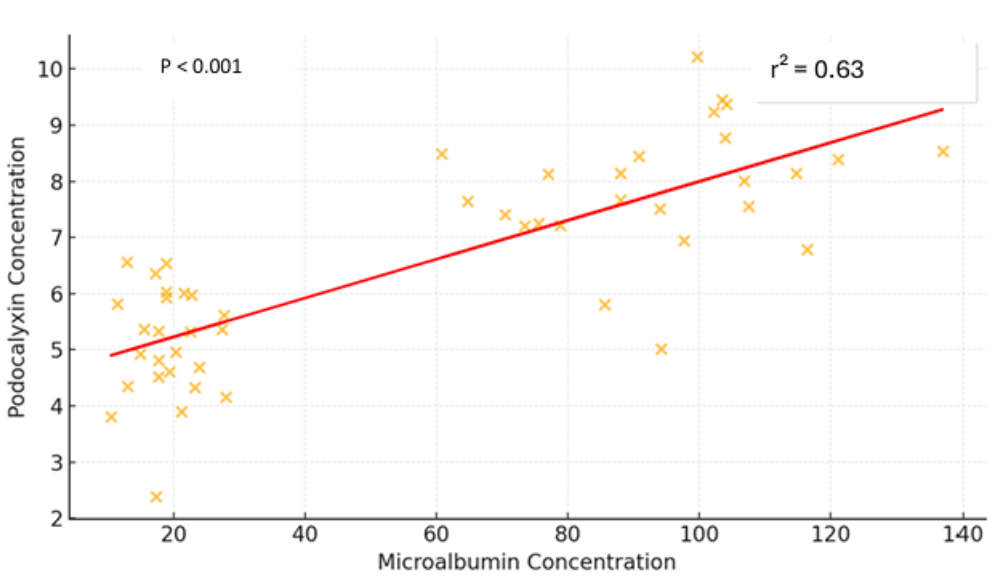

Figure 5: Correlation between urinary podocalyxin and urinary microalbumin

Figure 5 demonstrates that urinary podocalyxin and urinary microalbumin have a positive correlation across the entire study population, and the two urine markers both rise at an equivalent rate with aggravation of the glomerular injury. This is consonant with the hypothesis that diabetic nephropathy loss of podocalyxin precedes and accompanies albuminuria.

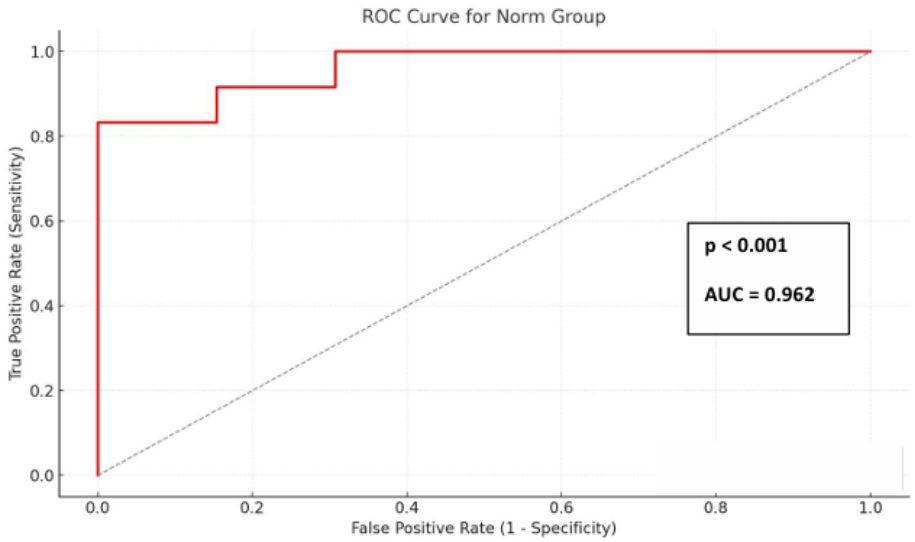

Figure 6: Receiver operating characteristic curve of urinary podocalyxin for detecting diabetic kidney disease in microalbuminuria

Figure 6 shows the ROC curve of urinary podocalyxin in identifying diabetic kidney disease in patients with microalbuminuria, with an AUC of 0.962, which shows almost excellent discriminatory capacity. The curve validates excellent performance of diagnosis at the chosen cut-off of 7.21 ng/mL.

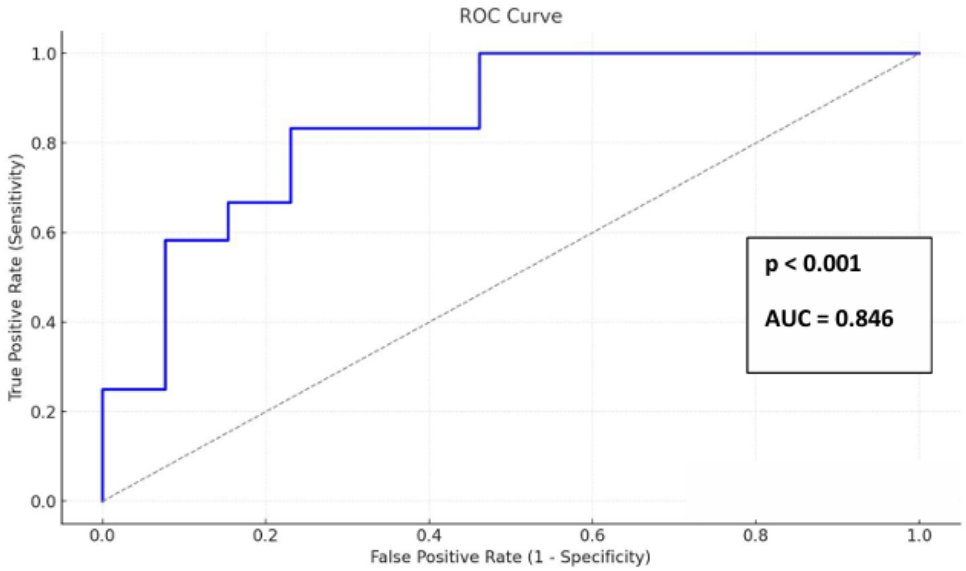

Figure 7: Receiver operating characteristic curve of urinary podocalyxin for detecting diabetic kidney disease in normoalbuminuria

The ROC curve of urinary podocalyxin in normoalbuminuric diabetic patients is presented in Figure 7 (AUC 0.846), and the diagnostic performance has shown to be good with a cut-off value of 3.04 ng/mL. This helps in the possibility of urinary podocalyxin in detecting early nephropathy, even in patients who do not show any sign of proteinuria.

Table 4 provides information on the diagnostic performance of urinary podocalyxin in ROC analysis. In the case of microalbuminuria, the AUC was 0.962 with 7.21 ng/mL as a cut-off, sensitivity was 79, specificity was 83.1, and accuracy was 81%. In normoalbuminuria, AUC was 0.846 with a cut-off of 3.04 ng/mL (sensitivity 71.2, specificity 86.4, accuracy 79.8), which again showed a high level of diagnostic utility between the two conditions of nephropathy.

Table 4: Diagnostic performance of urinary podocalyxin in detecting microalbuminuria and normoalbuminuria (N = 50)

Parameter	Microalbuminuria	Normoalbuminuric
AUC	0.962	0.846
Standard Error	0.041	0.057
Cut-off Value	7.21	3.04
Sensitivity (%)	79	71.2
Specificity (%)	83.1	86.4
PPV (%)	82.4	69.2
NPV (%)	79.8	87.5
Accuracy (%)	81	79.8
p-value	<0.001	<0.001

IV. DISCUSSION

This study assessed the diagnostic value of urinary podocalyx (uPCX) in diabetic nephropathy patients by stratifying them according to albuminuric status. The main results confirm that urinary podocalyxin is highly increased in diabetic patients with microalbuminuria in comparison with normoalbuminuric (7.89 ± 1.13 ng/mL vs. 5.11 ± 0.99 ng/mL, p<0.001), and that uPCX has an excellent diagnostic value in identifying diabetic kidney disease in the two stages. Demographic comparability was assured because the mean age in both groups was close to 51 years and was not statistically significant. BMI was also greatly higher in the microalbuminuric group (25.93 ± 4.61 vs. 23.83 ± 3.15 kg/m 2, p=0.032), which is in line with the already known interrelationship between obesity, insulin resistance, and the development of nephropathy. These results are consistent with reports by González-Pérez et al., who indicated that the components of metabolic syndrome are complementary to glomerular injury in diabetic patients [11]. As anticipated, the Group I (HbA1c of 8.60 +0.99) had higher levels than the Group II (HbA1c of 5.97 +0.38), which showed worse glycemic control in the microalbuminuric group. In the same manner, serum creatinine was elevated, and eGFR was very low in Group I, as de Boer et al. showed progressive deterioration in renal function with aggravating albuminuric conditions [12]. These biochemical

variations confirm our group assignment and confirm that microalbuminuria is a good predictor of more advanced nephropathic injury in this group. An important finding is that urinary podocalyxin is significantly high in microalbuminuric diabetic patients. Lioudaki et al. showed that urinary podocyte excretion is highly enhanced in diabetic nephropathy and is associated with the extent of urinary albumin excretion [13]. Equally, Fishea (2015) emphasized that podocalyxin, which is a podocyte-specific molecular marker, exhibits glomerular epithelial damage at an earlier stage than traditional biomarkers [14]. This has a biological cause in that, when exposed to conditions of hyperglycemia and hemodynamic stress that are typical of diabetic nephropathy, podocalyxin is detached and shed by the injured podocyte foot processes [15]. The analysis of the ROC curve revealed excellent diagnostic accuracy of urinary podocalyxin in the detection of microalbuminuria with an AUC of 0.962 at a cut-off of 7.21 ng/mL, a sensitivity of 79, a specificity of 83.1, and a total accuracy of 81. According to Zheng et al., mRNA expression by the urinary podocytes was able to distinguish the stages of different nephropathy and the more recent proteomic research has established that uPCX is more diagnostic than albuminuria as a diagnostic test [16]. The AUC of normoalbuminuric diabetic nephropathy was 0.846 (cut-off 3.04 ng/mL), indicating that podocalyxin may also be used to detect subclinical glomerular injury in patients without perceptible proteinuria. This observation has major clinical implications. Non- albuminuric diabetic kidney disease is also considered a different phenotype, and it is present in as many as one-third of patients with decreased eGFR with no microalbuminuria that can be detected [17]. Conventional screening methods that only use microalbumin screening have the risk of missing out on these patients. We indicate that urinary podocalyxin, which has 71.2 and 86.4 sensitivity and specificity, respectively, in the normoalbuminuric group, may be a useful adjunct variable in the early diagnosis of the disease in this underdiagnosed group [18]. The positive correlation of Urinary podocalyxin with HbA1c and urinary microalbumin and the significant negative correlation with eGFR support the biological plausibility of urinary podocalyxin as a disease-relevant urinary biomarker. Correlations of this nature have also been observed in pediatric and adult cohorts with diabetes, which further supports the generality of uPCX as a potential biomarker of nephropathy in a wide range of populations [19]. Making the urine collection technique non-invasive, stability of podocalyxin at standard storage temperatures, and the presence of validated ELISA platforms render this biomarker especially appropriate to be used in daily clinical practice [20]. The findings indicate that including urinary podocalyxin in the nephropathy screening tool could positively influence the diagnosis of nephropathy at an early stage, improve the promptness of nephroprotective medications, and possibly decrease the number of cases of ESRD under resources constraints [21].

Study Limitations: The sample size used in this study is relatively small, and it is a cross-sectional study with only one center thus it is not generalizable and does not allow the use of causal inference or the evaluation of the disease progression over time.

V. CONCLUSION

Urinary podocalyxin is a strong, non-invasive biomarker that precisely indicates the extent of podocyte damage in diabetic nephropathy. Our analysis indicates that the urinary podocalyxin levels are significantly higher in patients with microalbuminuric diabetes than in their normoalbuminuric counterparts, with excellent diagnostic performance as verified by ROC analysis. It is worth noting that urinary podocalyxin was also able to detect subclinical glomerular injury in normoalbuminuric patients, who are often overlooked by standard screening. The good correlations with eGFR, HbA1c, and urinary microalbumin demonstrate its biological significance. The inclusion of urinary podocalyxin in the regular screening procedures of nephropathy can help to diagnose promptly, intervene, and eventually lead to a better clinical outcome among diabetic patients at risk of developing progressive kidney disease.

Recommendations: Multicenter prospective studies should be conducted in the future with larger sample sizes to confirm these results, define population-specific reference ranges, and find out whether urinary podocalyxin can predict the development of advanced diabetic kidney disease.

References

[1]. Tuttle KR, Bakris GL, Bilous RW, Chiang JL, De Boer IH, Goldstein-Fuchs J, Hirsch IB, Kalantar-Zadeh K, Narva AS, Navaneethan SD, Neumiller JJ. Diabetic kidney disease: a report from an ADA Consensus Conference. Diabetes care. 2014 Oct 1;37(10):2864-83.
[2]. Atlas D. International diabetes federation. IDF Diabetes Atlas, 7th edn. Brussels, Belgium: International Diabetes Federation. 2015;33(2):3-6.
[3]. Reidy K, Kang HM, Hostetter T, Susztak K. Molecular mechanisms of diabetic kidney disease. The Journal of clinical investigation. 2014 Jun 2;124(6):2333-40.
[4]. Barutta F, Bellini S, Gruden G. Mechanisms of podocyte injury and implications for diabetic nephropathy. Clinical Science. 2022 Apr;136(7):493-520.
[5]. Nielsen JS, McNagny KM. Novel functions of the CD34 family. Journal of cell science. 2008 Nov 15;121(22):3683-92.
[6]. Hara M, Yanagihara T, Kihara I. Cumulative excretion of urinary podocytes reflects disease progression in IgA nephropathy and Scho [Combining Diaeresis] nlein-Henoch purpura nephritis. Clinical Journal of the American Society of Nephrology. 2007 Mar 1;2(2):231-8.

[7]. MacIsaac RJ, Jerums G. Diabetic kidney disease with and without albuminuria. Current opinion in nephrology and hypertension. 2011 May 1;20(3):246-57.
[8]. Zheng M, Lv LL, Ni J, Ni HF, Li Q, Ma KL, Liu BC. Urinary podocyte-associated mRNA profile in various stages of diabetic nephropathy. PLoS One. 2011 May 31;6(5):e20431.
[9]. Lioudaki E, Stylianou KG, Petrakis I, Kokologiannakis G, Passam A, Mikhailidis DP, Daphnis EK, Ganotakis ES. Increased urinary excretion of podocyte markers in normoalbuminuric patients with diabetes. Nephron. 2015 Sep 5;131(1):34-42.
[10]. Gluhovschi C, Gluhovschi G, Petrica L, Timar R, Velciov S, Ionita I, Kaycsa A, Timar B. Urinary biomarkers in the assessment of early diabetic nephropathy. Journal of diabetes research. 2016;2016(1):4626125.
[11]. González-Pérez A, Sáez M, Vizcaya D, Lind M, Rodriguez LG. Incidence and risk factors for mortality and end-stage renal disease in people with type 2 diabetes and diabetic kidney disease: a population-based cohort study in the UK. BMJ open diabetes research & care. 2021 Oct 4;9(1).
[12]. de Boer IH, Rue TC, Hall YN, Heagerty PJ, Weiss NS, Himmelfarb J. Temporal trends in the prevalence of diabetic kidney disease in the United States. Jama. 2011 Jun 22;305(24):2532-9.
[13]. Lioudaki E, Stylianou KG, Petrakis I, Kokologiannakis G, Passam A, Mikhailidis DP, Daphnis EK, Ganotakis ES. Increased urinary excretion of podocyte markers in normoalbuminuric patients with diabetes. Nephron. 2015 Sep 5;131(1):34-42.
[14]. Fiseha T. Urinary biomarkers for early diabetic nephropathy in type 2 diabetic patients. Biomarker research. 2015 Jul 4;3(1):16.
[15]. Fakhruddin S, Alanazi W, Jackson KE. Diabetes-induced reactive oxygen species: mechanism of their generation and role in renal injury. Journal of diabetes research. 2017;2017(1):8379327.
[16]. Zheng M, Lv LL, Ni J, Ni HF, Li Q, Ma KL, Liu BC. Urinary podocyte-associated mRNA profile in various stages of diabetic nephropathy. PLoS One. 2011 May 31;6(5):e20431.
[17]. MacIsaac RJ, Ekinci EI, Jerums G. Progressive diabetic nephropathy. How useful is microalbuminuria?: contra. Kidney international. 2014 Jul 1;86(1):50-7.
[18]. Laranjinha I, Matias P, Mateus S, Aguiar F, Pereira P, Santos MP, Costa R, Lourenço A, Guia J, Barata JD, Campos L. Diabetic kidney disease: Is there a non-albuminuric phenotype in type 2 diabetic patients?. Nefrología (English Edition). 2016 Sep 1;36(5):503-9.
[19]. Akankwasa G, Jianhua L, Guixue C, Changjuan A, Xiaosong Q. Urine markers of podocyte dysfunction: a review of podocalyxin and nephrin in selected glomerular diseases. Biomarkers in medicine. 2018 Aug 1;12(8):927-35.
[20]. Wang G, Lai FM, Kwan BC, Lai KB, Chow KM, Li PK, Szeto CC. Podocyte loss in human hypertensive nephrosclerosis. American journal of hypertension. 2009 Mar 1;22(3):300-6.
[21]. Wang G, Lai FM, Kwan BC, Lai KB, Chow KM, Li PK, Szeto CC. Podocyte loss in human hypertensive nephrosclerosis. American journal of hypertension. 2009 Mar 1;22(3):300-6.