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Nephrin: An Early Biomarker of Diabetic Nephropathy Among Type- 2 Diabetic Patients in Kano Metropolis**Ahmad M. B. ^{*1}, Adamu A. I. ¹ and Sarafa O.O ²**Department of Medical Laboratory Science, BUK, Kano ¹, Medical Laboratory Unit, Bayero University Clinic, BUK, Kano ²Author for Correspondence*: ambello.mls@buk.edu.ng. <https://dx.doi.org/10.4314/sokjmls.v10i4.16>**Abstract**

Nephrin as a trans-membrane protein was reported to be expressed in glomerular podocytes having a fundamental role in the integrity of glomerular filtration barrier. Nephriuria was reported in podocytopathy, hence, could serve as an excellent emerging biomarker in early diagnosis kidney injury and chronic diseases. The study assessed nephrin as early biomarker in detection of diabetic nephropathy among type 2 diabetic patients in Kano metropolis. The study was a case- control and included 120 diabetic patients including 43 males and 77 females, from endocrinology clinic of Murtala and Nassarawa Specialist Hospitals, Kano with corresponding 100 apparently healthy controls. Fasting blood glucose, albumin, glycaeted-haemoglobin and creatinine were determined spectrophotometrically, while urinary nephrin was estimated using ELISA technique. eGFR was estimated using simplified MDRD equation. Student t-test compared the differences between the two groups and regression analysis was used to correlate between nephrin and ACR and HbA1c. A receiver operating characteristic (ROC) curve was used to assess the sensitivity, specificity and area under the curve (AUC) of the analytes. Nephrin, serum creatinine, albumin level in urine and the glycaeted-haemoglobin were significantly elevated in Type-2 diabetic patients compared to controls ($p=0.001$). Negative and significant correlation was seen between glomerular filtration rate (eGFR) and nephrin ($r = -0.61, p=0.001$) while a significant but positive correlations between nephrin vs ACR ($r=+0.70, p=0.001$) and glycaeted-haemoglobin ($r = +0.59,$

$p=0.001$). The urinary Nephrin presented a better diagnostic accuracy with sensitivity of 97.7% and specificity of 63.2% as well as AUC of 0.872. Results demonstrated that nephrin was superior to traditional marker of renal function, better sensitivity and specificity. Thus, nephriuria is a promising and better marker than ACR for predicting early onset of nephropathy especially glomerular injury in patients with T2DM.

Keywords: Neprin, albumin-creatinine ratio, Diabetic nephropathy, podocyte**Introduction**

An estimated 589 (11.1%) 853 million (13%) by 2050 among adults aged 20–79 years living with diabetes of the world's population. About 252 million adults living with diabetes are unaware having DM. Spending over 1 trillion USD (12%) on diabetes in 2024 of global health expenditure. Death toll of over 3.4 (9.3%) million people as a result of diabetes in 2024 of global deaths from all causes.

The gold standard, ACR, for early detection of DN has several limitations, therefore, earlier and more sensitive and specific biomarkers with greater predictability are needed. Diabetic nephropathy (DN) is a leading cause of end-stage renal disease (ESRD) in developed countries (IDF, 2025). DN is associated with persistent albuminuria, decline in glomerular filtration rate (GFR), raised arterial blood pressure and increased cardiovascular mortality (Peter *et al.*, 2018; Pugliese *et al.*, 2019; Batuman *et al.*, 2024).

Nephrin is a podocyte-specific glycoprotein that plays an essential role in the structure of the filtration diaphragm in the glomerulus and provides the ultimate physical barrier for plasma proteins. Nephrin is one of the excellent emerging biomarkers for early detection of diabetic nephropathy (ElNagar, 2022). Microalbuminuria, which is considered as a gold standard in early detection of DN has several limitations. Therefore, earlier, more sensitive and specific biomarkers with greater predictability are needed. Early detection of DN will be of importance to mitigate progression to ESRD especially in LMIC as Nigeria, where facilities are costly or not available. Local data of nephrin as an early marker of DN is scanty compared to other biomarkers. Management can be initiated more aggressively at much earlier stage.

Study area

The study was conducted in the endocrinology unit of Murtala Muhammad and Abdullahi Wase specialist Hospitals, Kano and analyzed in the Department of MLS, BUK/CIDR

Study population

The study was a case control design involving 220 subjects consisting of 120 type-2 diabetic patients and 100 apparently healthy non-diabetic subjects serving as study controls.

Inclusion criteria: Type 2 diabetic patients, apparently healthy control, Age range of 20-79 years

Exclusion criteria: Pregnant women, CVD patients, Women in their menstrual cycle

Ethical consideration

An approval for the study was obtained from Ministry of Health Kano Research Ethics Committee. The purpose and scope of the study was explained clearly to the clients language understood well by the participants and informed consent was obtained and duly signed by all participants before proceeding with the study

Administration of Questionnaire

A set of questionnaires was developed and administered to each subject to obtain sociodemographic data, medical history and duration of diabetes.

Sample Size Determination

The number of samples used in the study was calculated using standard epidemiological formula for the determination of minimum sample size by Sarmukaddam and Gard (2006) as outlined below:

- $n = Z^2 pq / L^2$
Where:
- n = minimum number of samples to be collected (sample size)
- Z = standard normal distribution at 95% confidence interval = 1.96 from the z-table
- p = prevalence rate of diabetes mellitus from recent past research or study = 5.8% (IDF, 2021) = 0.058
- $q = 1 - p$
- L = allowable error of 5% = 0.05, so that relationship between variables will be significant

$$n = \frac{Z^2 \times p \times q}{L^2}$$

$$n = \frac{(1.96)^2 \times 0.058 \times (1 - 0.058)}{(0.05)^2}$$

$$n = 84$$

The minimum sample size was calculated 84 but consider 120 for more statistical power and 100 subjects (apparently healthy) were enrolled as control.

Ethical consideration

Ethical approval for the study was obtained from Ministry of Health Kano Research Ethics Committee

Statistical Analysis

Data obtained were analyzed using the Statistical package for Social Sciences (SPSS) programmed version 21 (Chicago, IL, USA). Analyses carried out were analyzed using descriptive statistics with mean and SEM or proportions, for continuous or categorical variables, differences were determined by Students *t*-test and ANOVA and p-values of less than 0.05 were considered to be significant. A Pearson product-moment correlation was conducted to determine the relationship between variables. ROC curve was used to determine clinical utility of nephrin to microalbuminuria in assessing early kidney injury.

Results

Table 1: Socio-demographic characteristics of study participants

Demographic Characteristic	n(%)
Gender	
Male	43 (35.8)
Female	77 (64.2)
Age group (years)	
21-30	3 (2.5)
31-40	21 (17.5)
41-50	37 (30.8)
51-60	33 (27.5)
61-70	19 (15.8)
71-80	7 (5.8)
Occupation	
Civil servants	36 (30.0)
Traders	12 (10.0)
Artisan/non-working	72 (60.0)
Educational status	
Tertiary	42 (35.0)
Secondary	7 (5.8)
Primary	12 (10.0)
Non formal education	59 (49.2)
Duration of illness	
>5 years	112(93.3)
=5 years	8(6.7)
Diabetic Nephropathy	
Normoalbuminuria	40(33.3)
Microalbuminuria	59(49.2)
Macroalbuminuria	21(17.5)
Nephrinuric	
Normoalbuminuria	28(23.3)
Microalbuminuria	57(47.5)
Macroalbuminuria	35(29.2)

Table 2: Comparison between biochemical indices among Type-2 DM and control

Groups	N	ACR (mg/g of Cr)	eGFR (ml/min/1.73m ²)	Nephrin (ng/L)	HbA1C (%)
NAIb	41	15.49±1.17 ^a	66.56±2.63 ^c	22.80±3.08 ^a	14.70±1.04 ^b
MiAlb	58	75.11±6.24 ^b	53.91±2.65 ^b	78.00±9.44 ^b	17.62±0.91 ^c
MaAlb	21	313.57±2.13 ^c	31.86±6.50 ^a	201.14±13.66 ^c	22.79±1.56 ^d
Control	100	20.86±0.60 ^a	77.58±0.67 ^d	10.00±0.24 ^a	5.32±0.19 ^a

Key: Results are expressed as mean ± SEM using one-way ANOVA statistical tool for analysis. Mean values with similar superscripts (a, b, c, or d) in the same column are not statistically significant (p>0.05) while those with different superscripts (a, b, c, or d) in the same column are statistically significant (p<0.05). NAIb=normo-albumin, MiAlb=micro-albumin, MaAlb=macro-albumin, ACR=Microalbuminuria, eGFR=Estimated Glomerular Filtration Rate

Table 3: Correlation between Nephrin and ACR, BMI, eGFR and HbA1c

Parameters	r-value	p-value
ACR	+0.65	0.001
BMI	+0.17	0.12
eGFR	-0.58	0.001
HbA1C	+0.60	0.001

Correlation analysis was done using spearman's correlation coefficient.

ACR= albumin to creatinine ratio, BMI= body mass index, eGFR=estimated glomerular filtration rate, HbA1c= glycaeted haemoglobin

Table 4: Relative Diagnostic Efficacy between Nephrin and ACR

Parameters	Sensitivity (%)	Specificity (%)	AUC (%)	p-value
ACR	73.4	60.6	0.657	0.001
Nephrin	97.7	63.2	0.872	0.001

ACR=albumin creatinine ratio, AUC=area under curve

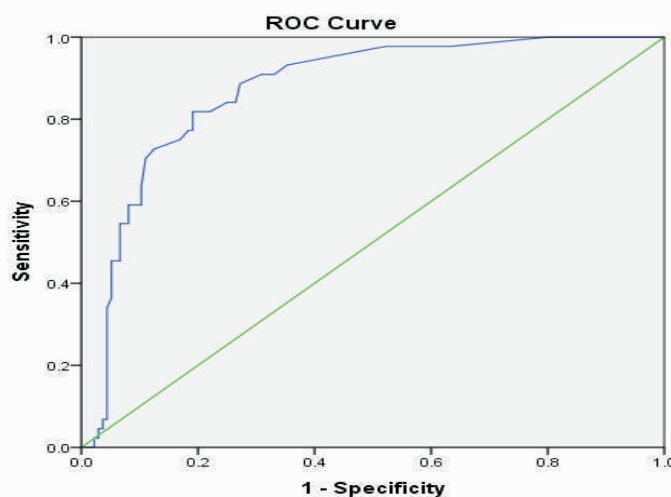


Figure 1: ROC of serum Nephrin as compared to UACR in Diabetic Nephropathy

Discussion

Early detection of DN is of paramount importance to provide appropriate therapy that will prevent evolution of diabetic nephropathy to end-stage renal disease especially among low- and middle-income countries such as Nigeria where facilities to cater for such patients are costly or not available.

The study observed marked gender difference with more female as compared to male. A study by Enikuomehin *et al.* (2020) revealed high number of females which might be attributed to willingness to visit hospitals and join the study. A study by Ramalan *et al.* (2021) reported otherwise with high number of males compared to female.

Considering the age of DM onset, the study observed higher prevalence in the middle age group as similarly reported by Ramalan *et al.* (2021) and Iwuagwu *et al.* (2023). This implied that earlier and aggressive intervention to prevent the development of disease complication will play a vital role in the nation's economy

Level of nephrin as observed in this study was significant even among normoalbuminuric when considering the definition of albuminuric subjects. Similar report was seen by Rangaswamaiah, (2022) who reported a significantly elevated level of urinary nephrin in normoalbuminuric subjects only when compared with ACR. Ganesh and Murugan, (2022) also observed marked significant increase in SCr, Ualb, ACR and nephrin and decline in eGFR among macroalbuminuric group. They also observed a proportional increase in urinary nephrin from normoalbuminuric to macroalbuminuric group attributed to structural alterations in podocytes.

Glycaeted haemoglobin was seen to significantly increase when compared with trend of glycaemic control from normal to poor control. This implies that urinary nephrin increases with poor glycemic control due to significant proteinuria associated with poor glycemic control in patients with diabetes resulting from development of kidney disease. Studies by Norris *et al.* (2018) and Li *et al.* (2024) observed an inverse relationship between protein excretion and GFR among T2DM patients.

It was noted in this study that diminution of GFR usually occurs after the development of microalbuminuria. In contrast, Kostovska *et al.* (2019) in Macedonia reported extremely high nephrin levels in all the groups. The different findings may be attributed to differences in ethnicity, diet, environmental and methodology used. Mesfine *et al.* (2023) and Yamanouchi *et al.* (2023) reported that both ACR and nephrin independently demonstrated decline in renal function, however nephrin showed higher sensitivity to renal function decline.

Conventionally, ACR has been the hallmark diagnostic tool for DN as observed in this study. ACR could not satisfy the criteria of early diagnosis of DN since it is not elevated in normoalbuminuria. The threshold of albuminuria varies greatly between individuals, hence DN can progress without significant albuminuria (Richard *et al.*, 2019). In support of this study, Kondapi *et al.* (2023) found that 51.1%, 85% and 100% of diabetic individuals with normoalbuminuria, microalbuminuria and macroalbuminuria respectively had increased nephrin. Reports from Irena *et al.* (2020) and Chittaragi *et al.* (2024) also agreed with our findings.

It is important to highlight that all macroalbuminuric patients exhibited advanced diabetic nephropathy in the study. The elevated concentration of urinary nephrin found in normoalbuminuric subjects indicated that damage of podocytes is present in subjects with T2DM before the appearance of microalbuminuria (Kandasamy *et al.*, 2014).

Conclusion: The level of nephrin is significantly high amongst diabetic patients with nephropathy. A strong correlation between nephrin with UACR, HbA1c and e-GFR was observed. Nephrin has proven sensitivity and specificity in diagnosing diabetic nephropathy considering the ROC result.

Recommendation: The use of urinary nephrin may be included as a diagnostic test for screening nephropathy in the management of diabetic patients. Large, prospective, multicenter and longitudinal studies are recommended to confirm the clinical utility of urinary nephrin for

renal progression in T2DM patients as predictor of DN in Nigeria.

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