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Renal Ultrasound and Renal Duplex Ultrasonography for Prediction of Diabetic Nephropathy in Correlation to Biochemical Markers & Glomerular Filtration Rate

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ABSTRACT

Background: Diabetic nephropathy represents a prevalent manifestation of chronic kidney disease (CKD) and stands as the most common microvascular complication observed among individuals with diabetes.

Objectives: This study aimed to investigate Doppler ultrasonographic parameters of the renal arteries in diabetic patients and to examine their correlation with renal function markers such as serum creatinine, estimated Glomerular filtration rate (eGFR), and proteinuria.

Patients and methods: A total of 300 adult diabetic patients were enrolled in this observational, cross-sectional study. Based on the progression of diabetic kidney disease, participants were stratified into three groups: Group I (preclinical stage) involved 56 individuals showing no clinical or biochemical signs of renal impairment, group II consisted of 88 patients with established diabetic nephropathy and group III that comprised 156 patients in the end-stage of diabetic renal disease.

Results: Group 3 patients exhibited a markedly higher left RI relative to groups 1 and 2 ($p < 0.001$). The left RI correlated positively and strongly with albuminuria ($r = 0.60$), urea ($r = 0.50$) and creatinine ($r = 0.65$), and HbA1c ($r = 0.45$) with high statistical significance ($p < 0.001$). A robust inverse correlation was observed between left RI and eGFR ($r = –0.68$, $p < 0.001$).

Conclusion: The renal resistive index (RRI) exhibited strong correlations with key biochemical markers, including albuminuria, creatinine, and HbA1c, while inversely correlated with eGFR across different stages of diabetic renal disease, which highlights the value of Doppler ultrasound as a non-invasive tool for early detection and monitoring of disease progression.

Keywords: Renal Duplex ultrasonography; Glomerular filtration rate; Diabetic nephropathy; Biochemical markers.

INTRODUCTION

Among the microvascular complications associated with diabetes, diabetic nephropathy is the most frequently encountered and constitutes a significant contributor to CKD. In many developing countries, it now stands as the foremost cause of end-stage renal failure. It is estimated that death due to renal disease is 17 times more common in diabetic than in non-diabetic patients [1, 2]. People with T2DM are at an increased risk of developing diabetic nephropathy (DN). The prevalence of DN in patients with T2DM is 30–40%, and DN accounts for 30–47% of new end-stage renal disease (ESRD) cases, increasing mortality from T2DM [3].

By impacting the entire vascular network, diabetes mellitus (DM) gives rise to a spectrum of complications involving both small and large blood vessels. Renal involvement in diabetic nephropathy is chiefly driven by atherosclerosis affecting intrarenal and extrarenal vessels, coupled with microvascular damage within the glomerular capillaries and arteriolar structures. Diabetic nephropathy is a well-known microvascular complication of diabetes [4].

Renal ultrasonography and Doppler studies are being used routinely in patients with azotemia as it is a non-invasive modality and to rule out possible obstructive uropathy, to measure the size of kidneys and to evaluate the renal parenchymal echogenicity [5].

This investigation aimed to determine whether intrarenal Doppler ultrasonography can serve as a reliable method for the early detection of DKD in individuals with type 2 diabetes. The study specifically examines the association between the renal resistive index and two principal biomarkers of DKD: Albuminuria and eGFR. Using intrarenal RI as a Doppler ultrasound indicator for DKD, a meta-analysis of RI versus albuminuria and RI versus eGFR was conducted to determine the usefulness of RI in predicting DKD [6].

Using Doppler ultrasonography, the RI is expressed as the ratio of the difference between the highest (systolic) and lowest (end-diastolic) flow velocities to the peak systolic velocity, based on measurements from the renal and intrarenal arteries. Duplex sonography provides an easily applicable, noninvasive, and well-established method for investigating renal functional or structural changes in diabetic nephropathy [7].

Elevated blood pressure, microalbuminuria and proteinuria can be considered as important signs of the progression of glomerular abnormalities in diabetic patients. Laboratory tests like urine protein, blood urea and serum creatinine have been traditionally used in clinical diagnosis and follow-up of diabetic nephropathy [8].

There are studies which showed the role of conventional ultrasound and Doppler evaluation of

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kidneys in the early detection of diabetic renal disease [9].

PATIENTS AND METHODS

This observational cross-sectional study was carried out at Beyla Hospital, Kafr AL-Sheikh governorate, and Benha University Hospitals through one year. This study included three hundred adult diabetic patients recruited from both Beyla and Benha University Hospitals.

Inclusion criteria: Diabetic patients, a clinically stable state at the time of evaluation, both sexes and age ≥ 18 years.

Exclusion criteria: Patients with active infections or underlying advanced malignancy, mental or physical problems interfering with study, overt thyroid disease, heart failure, and advanced COPD, renal artery stenosis, pregnancy, chronic liver disease complicated by ascites and patients who refused to participate in the study.

Grouping: Based on the clinical progression of diabetic renal disease, patients were stratified into three groups: Group I (Preclinical) comprised 56 diabetic individuals without signs of renal impairment, group II included 88 patients diagnosed with diabetic nephropathy and group III that included 156 cases of end-stage diabetic nephropathy.

All studied cases were subjected to the following: Detailed history taking [Personal history; age, gender, residence, occupation, socioeconomic status, and special habits, primary disease (Asking about the type of diabetes and any complaint such as dysuria or oliguria), past medical history, past surgical history: the participants were asked about any previous surgeries and family medical history].

Full clinical examination:

General examination [Heart rate, systolic blood pressure, diastolic blood pressure, respiratory rate and oxygen saturation], **Local examination** [Renal examination].

Laboratory investigations [Complete Blood Count (CBC), sodium, potassium, chloride, bicarbonate, lipid profile, kidney function tests, albumin, complete urine analysis, proteinuria assessment, fasting glucose, 2hr postprandial blood sugar, HbA1c and liver function tests].

Imaging [Conventional renal ultrasound, and renal artery doppler].

Renal artery Doppler study: To calculate resistive index using the following equation: Resistive index (Pourcelot index) = peak systolic flow velocity (cm/s) – (End diastolic flow velocity (EDV) (cm/s) / Peak systolic flow velocity (PSV)) (cm/s).

RI=PSV-EDV/PSV

A 3.5 MHz convex array ultrasound probe was used to assess both kidneys. The patient lay in a supine position while the radiologist, positioned to the right, applied the probe to the flank in an oblique approach to obtain longitudinal kidney images. The right kidney was visualized trans-hepatically, with the transducer angled appropriately in cases of reduced liver size. To overcome bowel gas interference with lower pole imaging, patients were placed in the right lateral decubitus position and scanned laterally. For the left kidney, imaging was performed with the patient in the left lateral decubitus position, arm extended overhead, using a coronal plane through the spleen. Bipolar length measurements of the kidney were typically taken during held inspiration.

The collected demographic data, metabolic and laboratory parameters, renal morphological measurements, and left renal doppler parameters were compared between all groups. Statistical analysis was done to study the correlation between resistive Index (RI) of renal artery and the following: Albuminuria, urea, cholesterol, eGFR, HbA1c, creatinine, renal length, renal parenchymal thickness, peak systolic velocity, and end diastolic velocity.

Ethical considerations: This investigation received ethical clearance from The Research Ethics Committee, Faculty of Medicine, Benha University. All subjects provided written informed consents prior to their participation. The consent process included explicit information about data use and publication, with guarantees of privacy and confidentiality. The study conformed to the principles of the World Medical Association's Declaration of Helsinki.

Statistical analysis

SPSS software version 21 (IBM Corp., Armonk, NY, USA) was used for statistical processing. Continuous data were presented as mean ± SD and analyzed using the Student's t-test or one-way ANOVA, depending on group structure. Categorical data were expressed as counts and percentages, with comparisons performed using Chi-square or Fisher's exact tests when applicable. A P value ≤ 0.05 (two-tailed) was deemed statistically significant.

RESULTS

Table (1) showed demographic data, distribution of diabetes type, urinary symptoms, overall metabolic and laboratory parameters, renal morphology and echogenicity and left renal Doppler parameters.

Table (1): Demographic data, distribution of diabetes type and urinary symptoms, overall metabolic and laboratory parameters, renal morphology and echogenicity and left renal doppler parameters

Age (years)		**66.81±6.22**	
Gender	Male	188 (62.7%)	
	Female	112 (37.3%)	
Type of Diabetes		Type 1	92 (30.7%)
		Type 2	208 (69.3%)
Dysuria		204 (68.0%)	
Oliguria		180 (60.0%)	
Laboratory Parameters			
Fasting Blood Sugar (mg/dl)		227.05 ±61.80	
PPBS (mg/dl)		397.25±14.31	
Hemoglobin (%)		9.46±2.22	
RBCs (10^6/µL)		4.47±0.32	
WBCs (10^3/µL)		11.70±2.25	
Platelet Count		126.87±29.33	
Albuminuria (mg/dl)		559.80±93.99	
Urea (BUN, mg/dl)		149.16±7.53	
Cholesterol (mg/dl)		271.79±57.21	
eGFR (ml/min)		36.48±2.90	
HbA1c (%)		8.76±1.21	
Creatinine (mg/dl)		4.58±0.50	
Renal Morphology			
Left Renal Length (cm)		10.24±0.71	
Right Renal Length (cm)		10.23±0.70	
Left Renal Parenchymal Thickness (mm)		6.04±0.81	
Right Renal Parenchymal Thickness (mm)		5.99±0.76	
Parenchymal Echogenicity		Normal	120 (40.0%)
		Increased	180 (60.0%)
Left Renal Doppler Parameters			
left Peak Systolic Flow Velocity (cm/s)		35.25±10.83	
Left End Diastolic Flow Velocity (cm/s)		7.98±2.67	
Left Resistive Index (RI)		0.88±0.14	

Data are presented as Mean±Std. Deviation or frequency (%)

The mean age significantly increases in group 3 in comparison with group 3 ($p = 0.018$). Gender distribution also significantly varied ($p = 0.000$). Similar significant differences were seen in the distribution of diabetes type, dysuria, and oliguria (all $p < 0.001$). Fasting blood sugar, PPBS, HbA1c, and creatinine progressively worsened from group 1 to group 3 (all $p < 0.001$). There were significant differences in left peak systolic flow velocity ($p = 0.000$), with group 2 showing the highest value, while the left end diastolic velocity did not differ significantly ($p = 0.241$). The left RI was markedly higher in group 3 relative to groups 1 and 2 ($p < 0.001$) (Table 2).

Table (2): Comparison of demographics, categorical variables, metabolic and laboratory parameters and left renal Doppler parameters between all groups

		Group 1	**Group 2**	**Group 3**	**p-value**
Age (years)		65.14 ± 6.04	66.27 ± 7.18	67.72 ± 5.55	0.018*
Gender	Male	48 (85.7%)	40 (45.5%)	100 (64.1%)	0.000*
	Female	8 (14.3%)	48 (54.5%)	56 (35.9%)	
Type of Diabetes	Type 1	32 (57.1%)	16 (18.2%)	44 (28.2%)	0.000*
	Type 2	24 (42.9%)	72 (81.8%)	112 (71.8%)	
Dysuria		8 (14.3%)	48 (54.5%)	148 (94.9%)	0.000*
Oliguria		0 (0.0%)	32 (36.4%)	148 (94.9%)	0.000*
Variable		Group 1	Group 2	Group 3	p-value
Fasting Blood Sugar (mg/dl)		214.71 ± 47.38	177.27 ± 48.66	259.56 ± 52.11	<0.001*
PPBS (mg/dl)		284.43 ± 7.98	335.64± 86.94	472.51 ± 49.51	<0.001*
Hemoglobin (%)		12.20 ± 1.01	10.55 ± 1.81	7.86 ± 1.17	<0.001*
RBCs (10^6/µL)		4.65 ± 0.24	4.39 ± 0.35	4.44 ± 0.31	<0.001*
WBCs (10^3/µL)		10.40 ± 2.14	11.46 ± 2.00	12.30 ± 3.29	0.001*
Platelet Count		158.29 ± 8.55	145.45± 37.02	105.10 ± 18.66	<0.001*
Albuminuria (mg/dl)		276.00 ± 29.65	362.18± 28.58	773.15 ± 45.07	<0.001*
Urea (BUN, mg/dl)		75.43 ± 11.26	119.09 ± 6.18	192.59 ± 6.08	<0.001*
Cholesterol (mg/dl)		210.86 ± 6.09	234.18 ± 17.62	314.87 ± 45.98	<0.001*
eGFR (ml/min)		60.61 ± 12.06	52.17 ± 5.88	18.96 ± 2.63	<0.001*
HbA1c (%)		7.57 ± 0.44	8.15 ± 0.46	9.54 ± 1.15	<0.001*
Creatinine (mg/dl)		1.79 ± 0.41	2.94 ± 0.08	6.51 ± 1.79	<0.001*
Left Renal Doppler					
Left Peak Systolic Velocity (cm/s)		34.97 ± 12.75	39.89 ± 9.31	32.73 ± 10.06	0.000*
Left End Diastolic Velocity (cm/s)		8.23 ± 2.51	8.26 ± 3.61	7.73 ± 2.02	0.241
Left Resistive Index (RI)		0.7243±0.0300	0.7991 ± 0.0216	0.9831 ± 0.1209	<0.001*

Data are presented as Mean±Std. Deviation or frequency (%), *: statistically significant as P value <0.05

Left RI showed strong positive correlations with albuminuria ($r = 0.60$, $p < 0.001$), urea ($r = 0.50$, $p < 0.001$), creatinine ($r = 0.65$, $p < 0.001$), and HbA1c ($r = 0.45$, $p < 0.001$), while it was strongly negatively correlated with eGFR ($r = –0.68$, $p < 0.001$). Additionally, there were weaker but significant correlations with renal length ($r = –0.20$, $p = 0.002$) and Doppler velocities (peak systolic $r = –0.15$, $p = 0.010$; end diastolic $r = –0.12$, $p = 0.030$), whereas the correlation with renal parenchymal thickness did not reach statistical significance ($r = –0.10$, $p = 0.070$) (Table 3).

Table (3): Bivariate correlations between left RI and biochemical parameters

Parameter	Pearson r	p-value
Albuminuria (mg/dl)	0.60	<0.001*
Urea (BUN, mg/dl)	0.50	<0.001*
Cholesterol (mg/dl)	0.30	<0.001*
eGFR (ml/min)	–0.68	<0.001*
HbA1c (%)	0.45	<0.001*
Creatinine (mg/dl)	0.65	<0.001*
Renal Length (cm)	–0.20	0.002*
Renal Parenchymal Thickness (cm)	–0.10	0.070*
Peak Systolic Velocity (cm/s)	–0.15	0.010*
End Diastolic Velocity (cm/s)	–0.12	0.030*

*: statistically significant as P value <0.05

Male patient 60 years old known as diabetic type 2 presented with fatigue, mild swelling in his feet over the past two weeks. He reported no significant changes in urination but mentioned occasional nocturia (Figure 1).

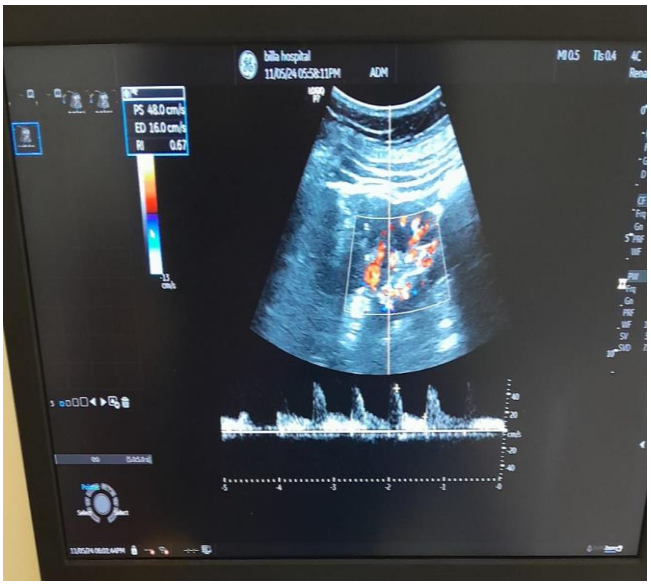

Figure (1): Male patient 60 years old known as diabetic type 2.

Female patient 55-year-old with advanced renal nephropathy with a history of T2DM, hypertension, and hyperlipidemia. She had diabetes for over 15 years, with poor glycemic control despite being on oral hypoglycemic agents and occasional insulin. She was diagnosed with CKD 5 years ago, and her kidney function had progressively declined. Over the past year, her kidney function worsened significantly, despite optimized management of her diabetes and blood pressure **(**Figure 2).

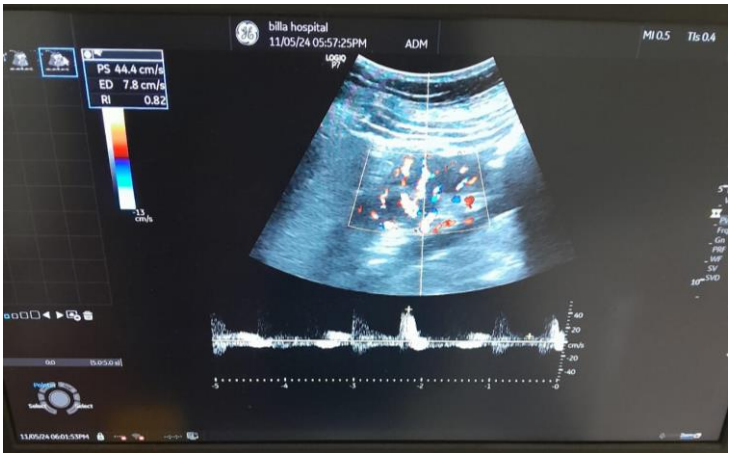

Figure (2): Female patient a 55-year-old with advanced renal nephropathy.

DISCUSSION

Our findings revealed significant metabolic and laboratory differences among diabetic patients at different stages of renal disease. Key parameters—fasting blood sugar, albuminuria, BUN, cholesterol, eGFR, HbA1c, and creatinine—worsened progressively from preclinical disease (Group 1) to end-stage nephropathy (Group 3). Unsurprisingly, group 3 showed the highest fasting blood sugar, HbA1c, Albuminuria, BUN and creatinine levels indicating worsened glycemic control and severe glomerular dysfunction. Additionally, eGFR declined significantly, confirming progressive renal insufficiency. Supporting our results, **Chen *et al.*** [10] in a study involving 992 CKD patients assessed by renal biopsy and Doppler ultrasonography, observed a marked reduction in renal size in individuals with stage 5 CKD relative to those in stages 1, 2, or 3. However, in the patients with stages 1–3 CKD, no significant association between the renal length and disease progression was identified, and the renal length showed a statistical but weak correlation with the renal function and histological damage scores.

The renal Doppler parameters revealed significant hemodynamic alterations in the left renal artery across different stages of diabetic renal disease. Interestingly, the left peak systolic velocity (PSV) was highest in group 2 compared to group 1, followed by an increase in group 3. This pattern may suggest a progressive disturbance in renal perfusion dynamics across different disease stages. The left end diastolic velocity (EDV) exhibited a slight reduction from group 2 to group 3. However, this difference did not reach statistical significance. This finding implies that while diabetic nephropathy was associated with altered renal blood flow patterns, EDV may be less sensitive than other Doppler parameters in detecting progressive renal impairment.

A notable observation is the significant increase in the left RI, which raised progressively from group 1 to group 2 and reaches its highest level in group 3. As a well-established indicator of intrarenal vascular resistance, the elevated RI in group 3 suggests severe renal hemodynamic dysfunction, likely attributed to increased vascular stiffness, diminished renal compliance, and advanced microvascular damage characteristic of end-stage diabetic nephropathy. Hence, incorporating Doppler ultrasonography may serve as a pivotal diagnostic and monitoring tool across different stages of diabetic renal disease.

Finally, our study demonstrated significant correlations between RI and key biochemical markers of renal function in diabetic patients, reinforcing the potential role of Doppler ultrasound as a non-invasive tool for assessing diabetic nephropathy. Notably, left RI exhibited strong positive correlations with albuminuria, urea, creatinine, and HbA1c, all of which were established indicators of renal dysfunction and glycemic control. The strongest correlation was observed between left RI and creatinine, reflecting the decline in renal filtration capacity as nephropathy progresses. Additionally, the significant positive correlation with albuminuria underscored the association between increased renal vascular resistance and glomerular injury. Conversely, left RI showed a strong negative correlation with eGFR, supporting its role as a marker of renal impairment. These findings indicated that increased RI may be associated with structural and hemodynamic alterations in the kidney. Overall, these findings highlighted the potential utility of Doppler ultrasound in conjunction with biochemical markers for the early detection and monitoring of diabetic nephropathy.

Consistent with our findings, a study conducted by **Abdelhamid *et al.*** [11] involving 60 type 2 diabetic patients with a disease duration of more than 5 years previous demonstrated a significant association between resistivity index (RI) and pulsatility index (PI) of renal arteries and the severity of albuminuria in patients with T2DM. participants were categorized into 3 groups based on their albumin/creatinine ratio (ACR) in the first voiding morning urine sample: Group I (ACR <30 mg/g creatinine), group II (ACR: 30–300 mg/g creatinine), and group III (ACR ≥300 mg/g creatinine). The study assessed ACR, serum creatinine, eGFR using the Cockroft–Gault formula, and HbA1c levels. RI and PI of the main renal and intrarenal arteries were measured bilaterally using duplex Doppler ultrasonography. The results indicated that RI and PI values were significantly higher in group III compared to group II and group I, ($P < 0.001$ for all comparisons). Furthermore, ACR demonstrated a strong positive correlation with RI and PI across all studied renal and intrarenal arteries ($P < 0.001$ for all). Similarly, a study conducted by **Mancini *et al.*** [12] reported that patients with higher RI values exhibited significantly greater proteinuria. Comparable findings were observed in studies by **Fallah *et al.*** [13] and **Hamano *et al.*** [14] further supporting the association between increased RI and worsening renal function. Additionally, **Masulli *et al.*** [15] demonstrated that patients with RI values exceeding 0.73 had a significantly higher baseline albumin excretion rate and experienced more frequent progression to advanced albuminuric states compared to those with RI values below 0.73. However, **Tsai *et al.*** [16] did not identify similar differences in RI values among three groups of adolescents and young adults with type 1 diabetes when categorized based on the severity of proteinuria. Supporting these findings, **Sperandeo *et al.*** [17] not only reported a comparable pattern but also identified a significant increase in RI—up to 0.91—among participants with elevated serum creatinine concentrations.

Although, the RI of normo- versus micro-albuminuria did not show significant change in the studies of **Thukral *et al.*** [18] and **Ozmen *et al.*** [19] they both reported a remarkable rise in the RI of all macroalbuminuria cases, which still supports that the RI increases with increasing albuminuria.

In a cohort of 64 diabetic patients, **Sharma *et al.*** [20] performed renal Doppler ultrasound targeting the main renal artery and interlobar arteries across the upper, mid, and lower kidney regions. The resistive and pulsatility indices were obtained for each artery, with mean values computed for each patient. These indices were then statistically correlated with HbA1c and serum creatinine levels. A robust and statistically significant correlation was noted between the mean RI and HbA1c ($r = 0.836$, $p < 0.001$), and Pearson's test was used to further assess the relationship between mean RI and serum creatinine. There was a strong, positive correlation between RI and serum creatinine, which was found to be statistically significant ($r = .859$, $p<0.001$) [20].

LIMITATIONS

Several limitations were considered when interpreting the findings of this study. The single-center design may compromise external validity, as differences in population characteristics and medical practice may affect the applicability of results to other settings. The cross-sectional approach also limits causal interpretation and does not allow for evaluation of temporal changes in renal function. Although the study included a statistically sufficient number of participants, the sample may not have captured the full clinical variability of diabetic nephropathy, thereby reducing sensitivity to detect less prominent associations.

CONCLUSION

The RRI exhibited strong correlations with key biochemical markers, including albuminuria, creatinine, and HbA1c, while inversely correlating with eGFR across different stages of diabetic renal disease, which highlighted the value of Doppler ultrasound as a non-

invasive tool for early detection and monitoring of disease progression.

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