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Renal Resistive Index as a Promising Tool in Early Identification of Diabetic Nephropathy

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ABSTRACT

Background: Diabetes mellitus (DM) is a common chronic illness that affects many persons all over the world. Diabetic nephropathy (DN) is a common serious problem that occurs in a considerable percentage of diabetic patients. Renal resistive index (RI) reflects hemodynamics of intrarenal arteries.

Objective: Here, we aimed to determine efficacy of RI in prediction of DN.

Patients and methods: A cross-sectional study was conducted over one year duration in Nephrology Unit of Internal Medicine Department, Assiut University Hospital. A total of 91 patients with DM were recruited. All patients were evaluated based on history taking, clinical evaluation, laboratory data and renal RI and subdivided into DN group and non-DN group.

Results: Out of those patients; 40 (43.9%) patients had DN (DN group) and 51 (56.1%) patients hadn't DN (No-DN group). Patients with DN had significantly longer duration of DM (10.45 ± 1.11 vs. 4.09 ± 0.56 (years); p< 0.001) and higher RI (0.89 ± 0.11 vs. 0.49 ± 0.18; *p*< 0.001). Duration of DM (> 5 years), impaired glycemic control and resistive index were predictors for DN among patients with DM. At cutoff point > 0.73, resistive index had 82.5% overall accuracy with area under curve was 0.837 for prediction of diabetic nephropathy.

Conclusion: Renal RI reflects hemodynamics of intrarenal arteries in patients with DM and could be used as a promising tool in early identification of DN. Multiple future studies at multiple centers with long term duration of assessment are warranted.

Keywords: Resistive index, Diabetic nephropathy, Diabetes mellitus, Accuracy.

INTRODUCTION

Diabetes mellitus (DM) is an important global public health concern, and type 2 diabetes mellitus (T2DM) in combination with renal dysfunction is linked to higher rates of cardiovascular and all-cause death. One of the most common and serious consequences of diabetes today is diabetic nephropathy (DN), which also continues to be the main cause of end-stage kidney disease (ESKD) globally [(1)].

Patients without DN often have a better prognosis and various therapeutic approaches. Because the pathological alterations of DN are thought to be difficult to reverse, it is considered that the patients' kidney results with DN are considerably poorer than those of their counterparts with biopsy-proven non-DN [(2)].

Renal Atrial Resistance Index (RI), which has been widely used to quantify Renal Blood Flow as a Semi-Quantitative Parameter, is easily and inexpensively measured using Doppler ultrasonography. Previous studies found a link between RI and the onset of a severe form of chronic kidney disease (CKD) with interstitial fibrosis [(3)].

In our locality we have a high prevalence of patients with DM with subsequent high percentage of those patients who are at risk to have CKD secondary to DN. But, there were insufficient data about role of RI in early detection of those patients with DN and so, this work aimed to evaluate such point.

PATIENTS AND METHODS

Study setting and design

A cross sectional study was conducted in the period between January 2021 to December 2021 in the Nephrology Unit of Internal Medicine department, Assiut University Hospital. A total of 91 diabetic patients were enrolled in the study. Out of those patients; 40 (43.9%) patients had DN (DN group) and 51 (56.1%) patients hadn't DN (No-DN group).

Inclusion criteria: All patients with DM were eligible for the study with age above 18 years old.

Exclusion criteria: Patients with known CKD, peripheral artery disease and/or severe comorbidities.

All patients were subjected to:

1- Though history taking and clinical evaluation (age, sex, duration of DM and type of therapy).
2- Complete blood picture, liver function panel, serum creatinine, blood urea nitrogen, urine analysis, and lipid profile were among the laboratory tests ordered.
3- Using the equation developed by the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI), the estimated glomerular filtration rate (eGFR) was calculated [(4)].

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4- Renal resistive index: The RI is computed using the formula RI = (peak systolic velocity - end diastolic velocity) / peak systolic velocity, may be used to measure blood flow resistance. In order to evaluate the size, shape, and echogenicity of the kidneys and rule out other renal illnesses, all of the chosen patients underwent a B-mode ultrasonographic examination of both kidneys. Additionally, a 3.5 MHZ convex transducer was used to examine the intra-renal arteries using colour Doppler ultrasonography.

After around three hours of fasting, patients were assessed in the prone position. The inter-lobar arteries were color-positioned before the Doppler sample volume was placed. Using a low wall filter and the lowest pulse repetition frequency possible without aliasing, all waveforms were measured on the largest Doppler scale possible. The transducer's angle was chosen to provide the clearest and largest waveform possible. Each vessel's three subsequent cardiac cycles were recorded.

The highest possible systolic and diastolic velocities were manually selected, and the integrated ultrasound unit software was then used to determine the RI. It was possible to acquire the waveforms of the RI of three vessels at various positions (upper, middle, and lower zones). The mean value for each kidney was then determined. Similar patterns and data were present in both the left and right kidneys in every subject. To prevent inter-observer variability, the same examiner conducted each and every Doppler test.

Ethical approval: The Academic and Ethical Committee of Assiut University approved the study on the 10th of October in 2018 (Approval No. 17200262). All participants received signed informed permission after being told of the study's goal. This study's execution was governed by the Declaration of Helsinki, the ethical standard for research involving human participants adopted by the World Medical Association.

Statistical analysis:

SPSS was used to gather and analyse the data (Statistical Package for the Social Science, version 20, IBM, and Armonk, New York). The mean and standard deviation (SD) of quantitative data were reported and compared using the Student's t test. Numbers (n) and percentages (%) were used to represent nominal data. Such data were subjected to the Chi Square test. The identification of potential risk variables for DN was done using multivariate regression analysis. The receiver operator characteristics (ROC) curve was used to assess the accuracy of RI in predicting DN. Since the level of confidence was maintained at 95%, a P value ≤ 0.05 was deemed significant.

RESULTS

Baseline data of patients based on DN (table 1):

Patients with DN had significantly longer duration of DM (10.45 ± 1.11 vs. 4.09 ± 0.56 years; p< 0.001) in comparison to those without DN. Other baseline data are of no significant value between both groups.

Table (1): Baseline data of patients based on DN

	DN group (n=40)	**Non-DN group (n= 51)**	***P* value**
Age (years)	51.56 ± 12.22	54.45 ± 15.55	0.34
Male sex	30 (75%)	39 (76.5%)	0.19
Duration of DM (year)	10.45 ± 1.11	4.09 ± 0.56	**< 0.001**
Therapy of DM			0.34
Insulin	15 (37.5%)	18 (35.3%)	
Oral agents	20 (50%)	23 (45%)	
Insulin/oral agents	5 (12.5%)	10 (19.7%)	
Family history of CKD	4 (10%)	6 (11.8%)	0.18
Type of DM			0.15
Type-1	15 (37.5%)	18 (35.3%)	
Type-2	25 (62.5%)	33 (64.7%)	

Baseline laboratory data of patients based on DN (table 2):

In comparison with the non-DN group, patients with DN had considerably lower levels of albumin and proteins as well as higher levels of random blood sugar, fasting blood sugar, and glycosylated haemoglobin.

Table (2): Baseline laboratory data of patients based on DN

	DN group (n=40)	Non-DN group (n= 51)	*P* value
Liver function tests			
Aspartate transaminase (u/l)	25 ± 6.12	19.52 ± 4.52	0.05
Alanine transaminase (u/l)	28.40 ± 6.52	25.92 ± 5.87	0.40
Bilirubin (µmol/l)	0.89 ± 0.21	0.88 ± 0.20	0.33
Albumin (mg/dl)	33.16 ± 5.99	37.52 ± 5.88	**0.01**
Proteins (mg/dl)	78.40 ± 7.82	68.89 ± 8.90	**0.03**
Complete blood picture			
Hemoglobin (g/dl)	11.40 ± 2.36	12.02 ± 1.61	0.19
Platelets ($x10^3$/ml)	320.28 ± 77.82	278.28 ± 66.42	0.11
Leucocytes ($x10^3$/ml)	5.76 ± 0.85	5.53 ± 1.10	0.64
Glycaemic control			
Random blood sugar (mg/dl)	259.08 ± 62.12	308 ± 72.32	**0.01**
Fasting blood sugar (mg/dl)	195.12 ± 46.28	219.12 ± 51.13	**0.04**
Glycosylated hemoglobin (%)	6.33 ± 0.98	9.04 ± 2.09	**< 0.001**
Kidney function tests			
Urea (mg/dl)	14.57 ± 1.09	15.19 ± 2.98	0.23
Creatinine (mg/dl)	0.99 ± 0.23	0.91 ± 0.22	0.64
Lipid profile			
Triglycerides (mg/dl)	134.87 ± 23.98	141.07 ± 32.53	0.15
Cholesterol (mg/dl)	189.98 ± 34.56	192.23 ± 47.21	0.29
LDL (mg/dl)	101.11 ± 24.13	99.11 ± 23.14	0.68
HDL (mg/dl)	41.41 ± 7.89	43.09 ± 5.21	0.98
INR	1.09 ± 0.04	1.08 ± 0.05	0.19

Resistive index among studied patients based on DN (table 3):

Patients with DN had significantly higher RI in comparison to those without DN (0.89 ± 0.11 vs. 0.49 ± 0.18; $p< 0.001$).

Table (3): Resistive index among studied patients based on DN

	Mean ± SD
DN group	0.89 ± 0.11
Non-DN group	0.49 ± 0.18
P value	**< 0.001**

Predictors for diabetic nephropathy among the studied patients (table 4): Based on this work; duration of DM (> 5 years), impaired glycemic control and resistive index were predictors for DN.

Table (4): Predictors for diabetic nephropathy among the studied patients

	Odd's ratio	95%CI	*P* value
Duration of DM (> 5 years)	2.99	1.88-4.50	**< 0.001**
Albumin (mg/dl)	0.45	0.22-1.01	0.33
Proteins (mg/dl)	0.90	0.70-1.89	0.90
Glycemic control	1.11	1.04-2.22	**0.01**
Resistive index	3.11	2.55- 7.78	**< 0.001**

Accuracy of RI in prediction of DN in the studied patients (table 5 and figure 1): At cutoff point > 0.73, resistive index had 82.5% overall accuracy with area under curve was 0.837 for prediction of diabetic nephropathy.

Table (5): Accuracy of RI in prediction DN in the studied patients

Indices	Value
Sensitivity	92%
Specificity	75%
Positive predictive value	74.3%
Negative predictive value	92.3%
Accuracy	82.5%
Cutoff point	> 0.73
Area under curve	0.837
P value	< 0.001

AUC: area under curve; DN: diabetic nephropathy.

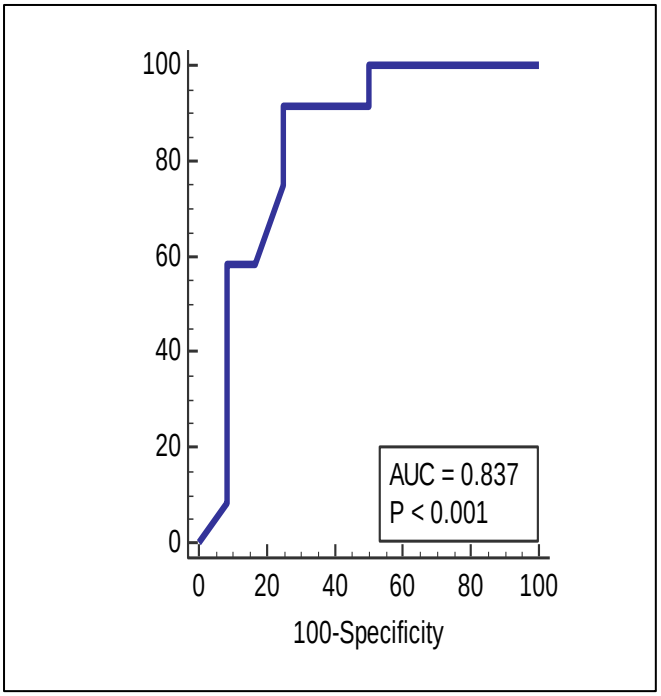

Figure (1): Receiver operator characteristics curve of resistive index for prediction of DN

DISCUSSION

There is presently no effective treatment for chronic kidney disease that can stop the disease from progressing or reverse the kidney function decline. One of the main causes of end-stage kidney failure is diabetic nephropathy. The increased oxidative stress in diabetic nephropathy, which affects the kidney's metabolic activity, metabolic pathways, and hemodynamic pathways, is primarily responsible for kidney damage [(5)].

Here, we tried to determine the renal RI's capacity for diagnostics in patients with DM for evaluation of those who are at risk for development of DN. The study included 91 diabetes patients in total. Out of those patients, 40 (43.9%) patients had DN (DN group) and 51 (56.1%) patients hadn't DN (No-DN group). The current study's primary conclusions were that 1) duration of DM (> 5 years), impaired glycemic control and resistive index were predictors for DN and 2) at cutoff point > 0.73, resistive index had 82.5% overall accuracy with area under curve was 0.837 in order to anticipate diabetic nephropathy.

DN is a serious sequel of DM that greatly affects outcome of those patients. Consistently with the current findings, DN occurs in up to 20-40% of patients with DM. Twenty percentage of DN may progress to end stage renal failure [(6-8)]. Additionally, similar with earlier studies, our study found that having diabetes for a long time is a significant risk factor for developing DN [(9-11)]. The duration of diabetes is often longer in DN patients than in control people. Diabetes history for at least five years is a risk factor for DN on its own [(11, 12)].

Another finding in this study was that patients with poor glycemic control are at risk for DN. There are findings that link better and more intense insulin administration, which improves the quality of diabetes care, to a general decrease in the incidence of diabetic vascular problems. At the very least, this might result in fewer serious difficulties down the road [(13, 14)].

The identification of reno-vascular disorders has made considerable use of the non-invasive, inexpensive Doppler ultrasonography technique. When segmental or interlobar arteries are used for Doppler spectrum analysis, the ratio of the difference between peak systolic velocity (PSV) and end-diastolic velocity (EDV) divided by PSV is used to compute RI [(11)]. According to a recent study, increased RI is a predictor for DN, which is consistent with our findings [(3)]. Recent research has shown that RI can accurately determine the status of renal blood perfusion, whether for renal disease brought on by diabetes and hypertension or for risk assessment and illness evaluation of early acute renal injury brought on by a variety of diseases [(11, 15-18)]. The study of **Rui *et al.*** [(14)] concluded that RI may be effective in detection of DN in type 2 - DM.

According to **Li *et al.*** [(11)]**,** the cutoff value of RI with the highest sensitivity (69.2%) and specificity (80.9%) for predicting DN was 0.66. In the multivariate logistic regression analysis for the prediction of DN, diabetic retinopathy, diabetes duration 60 months, glycosylated haemoglobin 7.0 (%), RI 0.66, and body mass index all shown statistical significance. Another studies determined cutoff > 0.70 as a predictor for DN [(19, 20)]. Regarding how RI and the severity of renal disease in people with diabetes interact, several prior studies have shown a favourable relationship between RI and proteinuria. The majority of people with RI 0.7 have severe proteinuria. The

increase in proteinuria, the more increase in the RI [8, 21, 22].

The present study's primary flaws were that it was a single-center study design, a limited sample size, and no long-term patients follow-up. Yet the main point of strength of this study being the first study discussed such issue in our locality.

CONCLUSION

Diabetic nephropathy is a common problem in diabetic patients. Resistive index of renal arteries could be used for early screening of patients who are at risk to develop DN. Future studies in multiple centers with larger sample size are suggested.

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