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ORIGINAL ARTICLE

Frequency of Diabetic Nephropathy, through Renal Resistive Index, among Type 2 Diabetic patients with Normal Albuminuria

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ABSTRACT

Background: The diabetes mellitus is an old known disease and closely related to the renal impairment as a cause. The exact duration for any damage to renal functions is not known but early detection of any such happening is a requirement. Many measures explain the renal damage, proteinuria is one among them. Still it appears after some damage is done.
Aim: To measure the RRI for renal arteries and find frequency of diabetic nephropathy among type II diabetic patients with normal albuminuria.
Methods: It was a cross-sectional study performed at Shaikh Zayed hospital Lahore, in collaboration of Diabetes Clinic and Radiology Department during January 2020 to January 2021. Here 300 diabetic patients of type 2, with normal albumin creatinine ratio were selected. Both genders with age above 18 years with albuminuria below 30 mg/g and no known diabetic nephropathy were included. Pregnant women, patients with GFR <60ml/min/1.73m^2 and those having any history of renal stones and known CKD patients were excluded.
Results: One hundred and seventy seven (59.0%) were males, only 38(12.7%) were above 60 years age, 37(12.3%) were obese and 180(60.0%) had duration of diabetes ≤5 years. There were 60(20.0%) smokers, 106(35.3%) had hypertension and 5.0% had fatty liver of grade III. On ultrasound 75(25.0%) cases had both kidneys with irregular contour while 44(14.7%) had raised Parenchymal & sinus echoes in both kidneys. On RRI, 23.3% of the cases were diagnosed to have diabetic nephropathy with max(RRI) >0.70.
Conclusion: Renal resistive indexcan diagnose diabetic nephropathy at early stage.
Keywords: Diabetic nephropathy, Renal resistivity index, Type II diabetes mellitus, Normal albuminuria

INTRODUCTION

Diabetes is the old known.[1] According to a diabetic survey of Pakistan 2016-17, the overall prevalence of diabetes was 23.6%, of which 19.2% were known diabetic whereas 7.1% were newly diagnosed diabetic[2].

Diabetes mellitus (DM) is a disease of poor in developed word and inunder-developed countries it is the disease of rich. It influences a larger population of the world, i.e. more than 220 million human beings, and is estimated to effect around 440 million during the year 2030[3]. Many complications in the form of organ damages due to DM are happening. DM affects the body from micro to macro vascular levels, by this way pressures of the body are also changed and the patient can also become hypertensive. Retinopathy, neuropathy, nephropathy are the main complications which are characterized on micro and macrovascularlevel[4].

Diabetic nephropathy (DN) is one of the main microvascular complications due to fibrosis and sclerosis of renal vessels and parenchyma.[5] DN is affected by defacing of the glomerular basement membrane, tissue damage of kidney due to hypoxia and causes not only narrowing of arterioles but also causes upper and lower urinary tract infections. These damages cause hypertrophy of kidney and dilatation of afferent arterioles. Due to dilatation of afferent arterioles filtration pressure in the glomerulus is increased and causes more damage to glomerular capillaries, increasing pressure also causes an increase in shearing forces at the local level which contributes to hypertrophy of mesangial cells and causes extracellular matrix secretion from mesangial cells which leads to glomerular sclerosis, initially basement membrane is thickened[6]. Destruction at such level results in leakage of large molecules of protein (mainly albumin), detected in urine, is called proteinuria (albuminuria) which can be on the micro or macro level and determine the initial damage of kidney[7].

Early detection of complications caused by T2DM, is necessary to prevent or control these complications. Different diagnostic modalities are used for the detection of complications caused by DM, some are laboratory-based such as kidney function tests (serum creatinine and blood urea levels), serum electrolytes, hormone analysis, lipid profile, serum protein, urinary protein (microalbuminuria) levels[9]. For T2DM patients, these should be checked on yearly basis. Morning spot urine should be checked for microalbumin level. Microalbuminuria is the albumin level in urine which can be detected on radioimmunoassay or with special urine dipsticks techniques[10]. Others relate to radiology such as duplex ultrasound (images for kidney size, shape and echotexture and Resistive index (RI) of renal vessels) and computed tomographic angiogram, magnetic resonance arteriogram, intravenous urography, and urodynamic studies[11].

A study conducted in Agha Khan hospital Pakistan constituted that renal size is communed to site of the kidney, gender, shape of body, body growths, age, it also concluded that sex and body mass index (BMI) are meaningful elementsand in adolescence, kidney size is 12.0 cm in length, 6.0cm in width and 3.0 cm in anteroposterior thickness and 77 to 94±22.0 cm^3 volume[12].

Ultrasound is a good diagnostic modality that can tell us the better and earliest idea about the complication happening in T2DM patients. It is a radiological modality that is harmless to the human body and is affordable and approachable and it can give the precise assessment of the kidney by giving proper sizes and texture and RI on color Doppler[13]. Findings of kidney disease on ultrasound are, reduction in cortical thickness (less than 6mm) and length of the kidney, raised parenchymal echoes and poor corticomedullary differentiation, irregular contours, the process of calcification in the papilla and renal cysts on the grayscale.[14]Doppler Ultrasound can also tell us the alteration in RI of renal vessels before the changes appear on clinical laboratory reports relate to renal function such as changes in the level of microalbuminuria. Findings of kidney disease on Doppler ultrasound are, reduction in cortical blush and raised RI values of interlobar and segmental arteries.[15]RI is the parameter to numerate the change in the vascular supply of renal parenchyma which can be found in renal disease. RI is closely related to

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abnormal elasticity of renal arteries. Renal RI of the segmental and interlobar artery is the most reliable and proved clinical parameter due to consistency in the result[16]. The average RI is 0.60±0.01 is normal and the cut off value is below 0.7 which shows the normal threshold[16,17]. Raising in RI value suggests that there is any structural abnormality or damage found in the Kidney. In many studies mean ranges of renal RI 0.50 to 0.64±0.05 are normal[18].

Italian study concluded that RI of renal arteries had the potency to detect DN, even before the blitz of microalbuminuria[19]. It also concluded that alteration in kidney volume and RI scores in DM patients are traceable on ultrasound. These alterations were seen in patients having signs of proteinuria and atherosclerosis with abnormal or controlled glomerular filtration rate (GFR) as well as enlarged kidney is also been observed among patients having diabetes with no proteinuria[20]. Egyptians performed a study on DM patients and concluded that there was an alteration in RI values of renal vessels in diseased and controlled patients and they found a meaningful connection between RI and DM span, serum creatinine value, and urinary albumin/creatinine ratio (ACR) and also evaluated that DN has a bad presage where the proportion of mortality is 40-100 times as compared to non-diabetics[21].

Keeping in view the above cited literature, this study was performed in local settings to see how RRI reflects kidney conditions among type 2 diabetic patients with normal albuminuria.

MATERIALS AND METHODS

It was a cross-sectional study performed at shaikh Zayed hospital radiology department in collaboration with diabetic clinic. A sample size of 300 was estimated with 95% confidence level, 3% margin of error with expected frequency of diabetic nephropathy on RRI>0.70 as 7.0%[19]. Cases of both genders, age above 18 years, albuminuria below 30mg/g and no known diabetic nephropathy were included. Pregnant women, patients with GFR <60ml/min/1.73m^2 and those having any history of renal stones and known CKD were excluded. For kidney ultrasound, patient came without any solid oral intake 6 hours prior to test and with full urinary bladder unless told to empty it. The test was performed on Renal Doppler ultrasound *machine* General Eletronics LogiqS7 *with linear* 6–10 MHz and curvilinear 2–5 MHz transducers. RI values of renal arteries (main, segmental and interlobar arteries), renal sizes and echo-texture were collected via pre-install software on Doppler ultrasound for both kidneys. The patients were examined in the supine, lateral or prone position with holding breath for maximum 10 to 15 second for Doppler ultrasound. Renal arteries, parenchymal texture and size on both sides were screened for any pathology. Images were obtained according to a standard protocol and radiological parameters were also recorded.

Data were entered and analyzed by using SPSS version 20.0. Results were presented by using frequency and percentages and renal resistive index were measured for each artery and presented by using median ($Q_1 – Q_3$). Left and right kidneys were compared for measurements by using Wilcoxon test and for contour and parenchymal & sinus echoes by using McNemar test. Frequency of DN was presented by using frequency and percentages for each artery as well as for maximum of the six artery readings. Any patient with RRI >0.70 was considered to have DN. P-value ≤0.05 was considered significant.

RESULTS

One hundred and seventy seven (59%) were male, 131(43.7%) had age below 45 years and 38(12.7%) had above 60 years. Majority (57.7%) had normal BMI and duration of diabetes was less than 5 years for 60% of the cases. Only 20% of them were smokers, almost one third had hypertension and 67% had no liver disease (Table 1).

The average measurements of left kidney for these cases were all significantly higher than the right kidney consistently. The major clinical difference was for median volume; for left kidney, it was 132.3(107.7–152.9) cm^3 while for the right kidney it was recorded 123.2 (101.6–145.6) cm^3, which was significantly different with p-value <0.001. (Table 2)

Table 1: Basic characteristics of cases evaluated for renal resistive index (n=300)

Variable		No.	%
Age	≤45	131	43.7
	46–60	131	43.7
	60$^+$	38	12.7
Gender	Male	177	59.0
	Female	123	41.0
BMI	≤ 25.0	173	57.7
	25.1-30.0	90	30.0
	30.0+	37	12.3
Duration of DM (Yrs)	≤5.0	180	60.0
	5.1-10.0	55	18.3
	10.1+	65	21.7
Smoking	Smoker	60	20.0
	Non smoker	240	80.0
Hypertension	Yes	106	35.3
	No	194	64.7
Liver grade	Grade-0	188	62.7
	Grade-I	66	22.0
	Grade-II	31	10.3
	Grade-III	15	5.0

Table 2: Measurements of right and left kidneys and their comparison

Measurement	Left kidney Median ($Q_1 – Q_3$)	Right Kidney Median ($Q_1 – Q_3$)	Wilcoxon test	
			Z	P-value
Length (cm)	11.5 (10.7–12.0)	11.5 (10.6–11.9)	5.95	<0.001
Width (cm)	4.8 (4.4–5.1)	4.6 (4.3–5.0)	8.86	<0.001
Thickness (cm)	4.6 (4.3–5.0)	4.5 (4.2–4.8)	6.37	<0.001
Volume (cm^3)	132.3 (107.7–152.9)	123.2 (101.6–145.6)	9.99	<0.001
Cortical thickness (mm)	11.0 (10.0–12.0)	11.0 (11.0–12.0)	2.84	0.005

The contours of left kidney were smooth for 210(70%) cases while for the right kidney 27.7% had irregular contour. There were 202(67.3%) of cases who had both kidneys with smooth contour and 75(25%) with both kidneys having irregular contour. There was no significant difference between left-side and right-side kidneys with p-value 0.210 (Table 3).

Table 3: Status and comparison of contours of two kidneys in each patient

Left	Right		Total
	Smooth	Irregular	
Smooth	202(67.3%)	8(2.7%)	210(70%)
Irregular	15(5%)	75(25%)	90(30%)
Total	217(72.3%)	83(27.7%)	300(100%)

P-value = 0.210

The parenchymal and sinus echoes were observed normal in both kidneys for 246(82%) of cases and raised in both for 44(14.7%). This difference between pair of kidney was also insignificant with p-value 0.344 (Table 4).

Finally when the frequency of diabetic nephropathy was observed on the basis of RRI reading for each artery, it was observed that the Interlobar artery of left kidney produced smallest percent of cases, i.e. 20(6.7%) with RRI>0.70. When

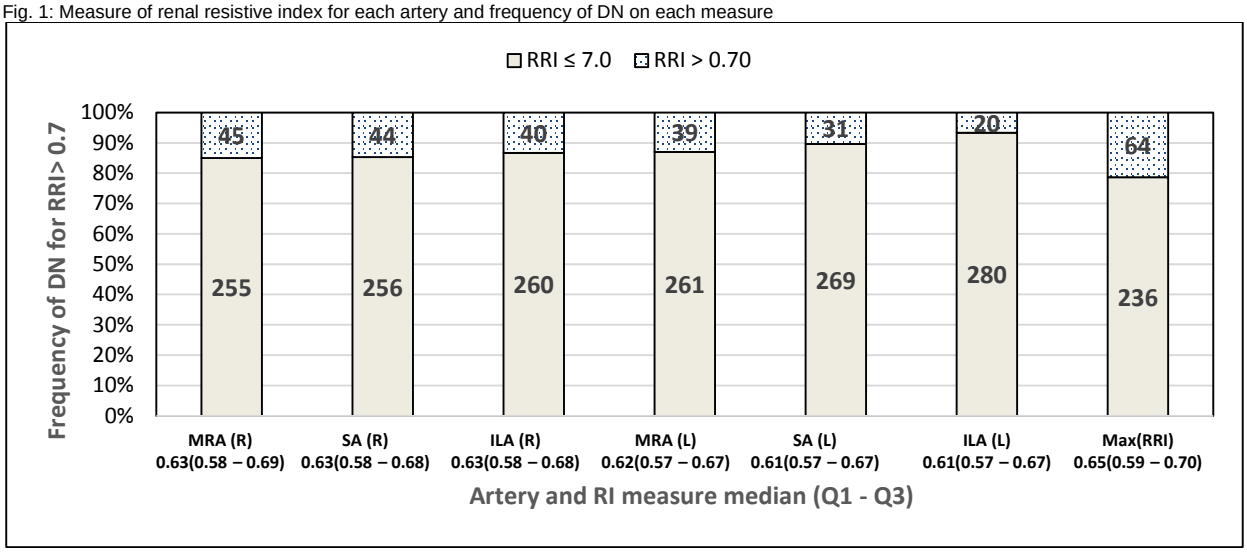
we considered other arteries as well, main renal artery of right had highest number, 45(15%) of cases, who had DN. Followed by segmental artery of right, interlobar artery of right, main renal artery of left, and segmental artery of left with 14.7%, 13.3%, 13.0% and 10.3% of the cases. Finally the maximum of the RRI for each case was considered and when DN was calculated on this basis, the number of cases with DN were quite high. In fact there were 64(21.3%) of cases which could be labeled to have DN on the basis of maximum RRI>0.70 (Fig. 1).

Table 4: Status and comparison of parenchymal and sinus echoes of two kidneys in each patient

Left	Right		Total
	Smooth	Irregular	
Normal	246(82%)	3(1%)	49(83%)
Raised	7(2.3%)	44(14.7%)	51(17%)
Total	253(84.3%)	47(15.7%)	300(100%)

P-value = 0.344

Fig. 1: Measure of renal resistive index for each artery and frequency of DN on each measure



DISCUSSION

Diabetes mellitus is one among the most common non-communicable diseases NCDs globally and DN is the most common microvascular complication of DM that occurs in approximately 30.0% of patients with DM. Microalbuminuria is recognized as an early marker of nephropathy and renal RI is a non-invasive predictor of nephropathy. The eGFR is commonly used to evaluate kidney function in CKD patients. But, it is challenging to assess the pathogenesis of CKD and predict the renal prognosis precisely using eGFR only. The renal RI by Doppler USG is considered a good marker of renal arterial resistance caused by atherosclerosis.

In a recently published cross-sectional observation study carried out at the Armed Forces Institute of Radiology and Imaging Rawalpindi Pakistan, Tahir et al. aimed to determine renal RI using Doppler USG in patients diagnosed with T2DM. The authors enrolled 150 T2DM patients and measured RI of both kidneys at the level of segmental arteries using the Doppler USG. Average RI was calculated by taking at least two readings for each upper, mid and lower pole. The mean age of 150 T2DM cases was 54.0±8.2 years. Among them, 58% patients were male and 42.0% female. This study also has 59% males. The means of duration of diabetes was 5.5±2.2 years, while in this study the mean duration id 6.6±6.5 years, indicates more variation in duration of diabetes in this study. This study also has a difference of selection of cases as, the selected cases were having normal albuminuria. The mean RI for left and right kidney were 0.72±0.02, 0.72±0.03 respectively, in this study the mean RRI at segmental artery for left and right kidney were 0.63±0.06 and 0.62±0.06. here in this study 14.7% had RRI >0.70 for right segmental artery and 10.3% on left segmental artery had above 0.70 which coordinates with the findings of that study, which concluded that high RI among T2DM patients suggest that renal RI by Doppler USG can be used as a non-invasive marker to identify T2DM patients who have higher risk of developing early nephropathy[22].

Another study by Toledo et al[11] also suggested that the cases with RRI≥0.70 had higher percentage of diabetic patients as compared to those with <0.70. This also indicates that RRI can be used as a marker for diagnoses of DN, though the study was performed to analyse RRI for CKD patients, while our study excludes CKD and hence more precise results for RRI to be an early diagnostic marker.

Stoyanova et al[7] summarized the results of another study and reported that all the groups with albuminuria >20 had average RRI of 0.70 or above which also indicates that RRI can be used as a marker of DN in diabetic patients at early stage. This study also gave 21.3% cases with maxRRI >0.70 and it coordinates with other literature.

CONCLUSION

Renal resistive index is a good marker for early diagnosis of DN and can save many patients going into complications caused by albuminuria raised in diabetic patients.

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