ORIGINAL ARTICLE

Correlation Between Renal Artery Resistive Index and Renal Function Tests in Type II Diabetic Patients

Maham Nasir[1], Sarah Maryam[2], Sadaf Abdul Qadir[3], Mehreen Fatima[4]

[1,3]Department of Medical Imaging & Ultrasonography, School of Health Sciences, University of Management and Technology, Pakistan;[2,4]University Institute of Radiation Sciences and Medical Imaging Technology, The University of Lahore, Pakistan

Corresponding Author: Maham Nasir, Department of Medical Imaging & Ultrasonography, School of Health Sciences, University of Management and Technology, Pakistan **Email:** mahamnasir302@gmail.com

Received: 20-04-2024
Revision : 06-07-2024
Accepted: 23-09-2024

ABSTRACT

Background: Diabetes has emerged as one of the major health care problems in Pakistan. It is also known that almost 50% of the people with diabetes remain undetected and some may even present with microvascular and macrovascular complications at the time of diagnosis. Diabetic nephropathy is a relatively common form of chronic renal disease.

Objective: The goal of the present research was to find the correlation between renal artery resistive index and renal function tests in individuals with type II diabetes.

Methods: This was a 9-month cross-sectional analytical study performed at Hamza Medicare Rahim Yar Khan in Pakistan, from April 2020 to December 2020. The research project comprised 60 people with type 2 diabetes mellitus who had been diagnosed with the disease for more than 5 years and had a HbA1c level of more than 6.5%. Patients had biochemical tests, a kidney examination, and a renal Doppler ultrasonography.

Results: Renal artery resistive index was increased in patients with high serum creatinine levels. Resistance index and serum creatinine had a positive correlation of r=0.438 (p<0.001). The correlation between RI and microalbuminuria was also positive, with r = 0.245 (p = 0.05). For r=-0.057 (p=0.663) there was a negative association between resistivity index and 24-hour urine protein. There was also a strong association between RI and HbA1c levels, with r=0.162 (p=0.217). correlation between RI and Duration of diabetes was significant with r=0.312 (p-value 0.015).

Conclusion: Therefore, it can be concluded that renal artery resistivity index assessed using duplex Doppler ultrasonography is a reliable method, which can be linked to the biochemical parameters of renal dysfunction in patients suffering from type 2 diabetes with diabetes and kidney disease.

Keywords: *Diabetic nephropathy, Doppler examination, microalbuminuria, 24-hour urine protein, proteinuria, resistance index, serum creatinine*

INTRODUCTION

In recent years, diabetes has become one of the most prevalent non-communicable diseases worldwide.[1,2] Among the adult population worldwide, about 21.9 million people suffered from diabetes mellitus (DM) according to the 2017 census, indicating a prevalence ratio of 1: 7 among people aged 20 and over. The percentages show that men and women are almost equally vulnerable to infection with this disease, women suffering 17.85% of cases, while men 16.22% of cases.[3] One of the chronic kidney disorders is diabetic nephropathy, which is characterized by albuminuria, which it goes to micro albuminuria and then macro albuminuria, and this can culminate to severe renal dysfunction.[4] Research indicates that RI values in segmental arteries accurately anticipate changes in distillate glomeruli. In non-insulin-dependent diabetes, glomerular sclerosis and mesangial thickening are the most common causes of renal involvement. RI is affected by fluctuations in vascular adherence and permeability in diabetic nephropathy.[5,6] Recently, many studies recognize the link between RI and biochemical parameters. Progression of kidney disease can be predicted using a high resistance index value. According to the study, renal resistance index is directly related to serum creatinine (R=0.729, p0.001) and 24-hour urine protein (R = 0.702, p0.001).[7] However, some reports suggested that interlobar segmental Doppler examination of the kidneys is as sensitive as the analysis of microalbuminuria in the urine in the detection of diabetic kidney disease.[8,9]

Ultrasonography and Doppler imaging were commonly used to diagnose chronic renal disease. The technique of Doppler ultrasonography can detect not only macro-scopic vascular irregularities in the kidney, as well as microvascular blood flow changes. Vascular conductance measurements at various points throughout the renal

parenchyma may reveal variations in the kidney's functioning or structural attributes.[10]

In one of the analysis it was found that the difference in diabetes period between normal albuminuric patient with RI<0.70 & RI>0.70 (p<0.05) was statistically significant but not significant for systolic blood pressure (p=1.000). An upsurge in RI can be seen before the development of microalbuminuria.[11] According to recent research, the progression of chronic kidney disease can be predicted by the value of RI. Based to this report, a high RI higher than 0.70 is related with the occurrence of chronic renal failure in the same way that proteinuria and hypertension are.[12] There is evidence that RI is associated with the rate at which reciprocal serum creatinine declines. Consequently, the index can be used to estimate the decline in renal function.[13] The raised RI (> or = 0.70) was related with worse renal function, greater proteinuria at twenty-four hours and a worse outcome. Sari et al. stated that intrarenal RI, which is strongly connected to blood creatinine concentration, might be utilized as a prognostic for individuals who have severe clinical diabetic nephropathy.[14]

Microalbuminuria predicts the emergence of macroalbuminuria and subsequent progression to clinically evident nephropathy in the course of the disease progression in later stages. Diabetic nephropathy progresses through stages marked by changes in glomerular blood pressure, enhanced vasoconstriction in renal arteries, and renal ischemia. Other people with chronic renal illness have shown a strong correlation between RI, filtration percentage and Effective renal plasma flow. The RI was also shown to be considerably higher in persons experiencing diabetes type 2 mellitus-related impaired kidney function compared to non-diabetic renal disease patients.[15]

Assessment of vascular structures using Doppler ultrasonography is a basic diagnostic tool that can also be used for organ assessment. Variations in intrarenal arterial waveforms can be used to identify hemodynamic changes. Color Doppler allows for faster and easier imaging, while duplex Doppler ultrasound enables quantifiable hemodynamic parameters.[16]

Previous studies have shown the importance of resistive index in intrarenal vessels. Current study will find out the importance of resistive index at the level of renal arteries. Doppler ultrasonography gives immediate results. Early changes in blood flow are picked up by renal Doppler and they reflect the progression of diabetic nephropathy.

METHODS

It was a nine-month cross-sectional analytical study. The study involved 60 type 2 diabetic patients who were more than 20 years old, had diabetes for more than five years and had an HbA1c level of more than 6.5 percent. Patients with high blood pressure, obesity, smoking, obstructive uropathy, individual or consensual small kidneys, congenital atypical kidneys, hereditary dyslipidemia, and renal masses were excluded. Patients' biochemical data such as serum creatinine, blood urea, microalbuminuria, 24-hour urine protein and HbA1c levels were collected during routine laboratory tests. Renal examination and renal Doppler ultrasound were performed at Hamza Medicare Rahim Yar Khan. Written informed consent was taken from all the participants. All information and data collection was kept confidential. Patients were scanned in supine position with 5 MHz linear probe placed along long axis of the main renal arteries through midline or flank approach. Spectral analysis of the aorta was made at the level of renal arteries. The velocity was taken with an angle for accurate measurement. Renal artery resistance index and kidney parameters were recorded. The final mean RI was calculated using the mean RI of both kidneys. SPSS 24.0 was used for data analysis. Descriptive statistics were provided for both qualitative and quantitative data. For quantitative data, the mean and standard deviation were reported. Quantitative data were used to represent qualitative variables. The Pearson correlation was applied to find the relationship of study variables. P-value <0.05 was considered to be significant.

RESULTS

Among the 60 patients, there were thirty six men (60%) and twenty four (40%) women aged between 21 and 54 years. Participants were categorized in groups according to duration of diabetes. Most of the patients were suffering from diabetes for more than 6 years (30%). Mean serum creatinine was calculated as 3.97$\pm$0.70, while mean blood urea 54.5$\pm$4.92, mean 24-hour urine protein 5.53$\pm$0.14, mean microalbuminuria 28.57$\pm$1.5, mean HbA1c 7.40$\pm$0.40 & mean resistance index 0.72$\pm$0.01 was recorded. (Table 1)

Table 2 show that the association between RI and biochemical parameters was determined using Pearson's correlation. Resistance index and serum creatinine had a positive correlation of r=0.438 (p=0.000). There was also a strong association between RI and HbA1c levels, with r=0.162 (p=0.217).

The sonographic examination of the kidney showed normal echo texture and normal corticomedullary differentiation in majority of the patients with percentage of 66.7%

Table 1: *Descriptive statistics of Biochemical Parameters*

Renal Function Tests	Minimum	Maximum	Mean	St. Deviation
Serum Creatinine	2.03	6.10	3.9773	.70828
Blood urea	35	69	54.5500	4.92460
24-h urine protein	1.90	26.10	5.5385	4.14367
Microalbunimurea	4.71	53	28.5747	8.57218
HbA1c	6.10	8.20	7.3515	.40928

Table 2: *Correlation between Renal Artery Resistive Index and Biochemical Parameters*

Renal Function Tests	Resistive Index	
	Pearson's correlation	Sign. (2-tailed)
Serum Creatinine	0.438	0.000
Blood Urea	0.575	0.000
Micro-albuminuria	0.245	0.05
24-Hour urine protein	-0.057	0.663
HbA1c	0.162	0.217

All the patients were divided in 3 groups on the basis of duration of diabetes. Group 1 included patients having diabetes from 5-7 years. Patients having diabetes for 8-9 years were placed in group 2 and group 3 included patients having diabetes for 10-15 years. Mean difference of resistive index between group 1 and 2 was -0.01386 and was significant with p-value<0.05. Mean RI difference between group 1 and 3 was -0.00338 and it was insignificant with p-value>0.001. Mean RI difference between group 2 and 3 was 0.01048 and it was also insignificant with p-value>0.001.(Table 3)

Table 3: *Mean Difference of Resistive Index with Respect to Duration of Diabetes*

Groups		Mean Difference	St. error	p-value
1	2	-0.01386	0.00455	0.003
	3	-0.00338	0.00613	0.583
2	1	-0.01386	0.00455	0.003
	3	0.01048	0.00682	0.130
3	1	-0.00338	0.00613	0.583
	2	0.01048	0.00682	0.130

Scatter plot show increasing trend i.e. positive relationship between renal resistive index and duration of diabetes (p-value 0.015). As duration increases resistive index also increases. (Figure-1)

These results showed that type II diabetes does not affect the renal parenchyma, but its effect on renal hemodynamics is quite evident, as the renal resistance index increases with increasing duration of diabetes.

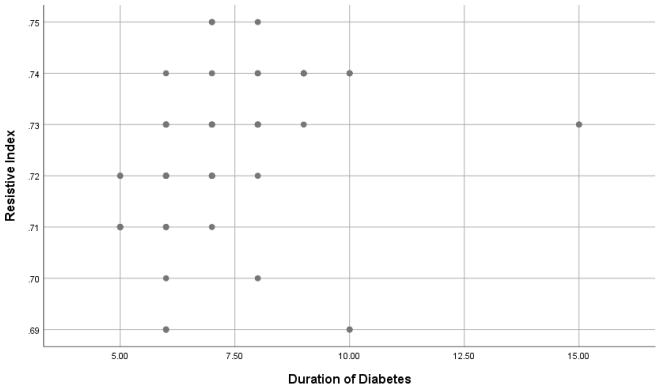

Figure 1: *Scatter plot of Resistive Index and Duration of Diabetes*

Moreover, changes in renal hemodynamics were consistently significant with changes in biochemical parameters.

DISCUSSION

Seven patients had an RI less than 0.70, while 53 had an RI greater than 0.70. RI was significantly associated with elevated serum creatinine 3.97±0.70 (p=0.000). The present findings were consistent with earlier work by Raut et al, who found that elevated serum creatinine was significantly associated with RI (2.29±1.46) (p=0.001).(17) Ghadirpour et al. also found increased Serum Creatinine (1. 65±0.41) and a strong connection with RI (p=0.039). There is a substantial association between RI and serum creatinine (r = 0.581; p < 0.01).[19] Platt et al. discovered that when a patient's intrarenal resistive index exceeds than 0.70, survival rates decrease. The average serum creatinine level was 3.2 mg/dl. The table below displays the breakdown of patients based on their mean serum creatinine level. 2 mg/dL. Samuel et al. [15] found a statistically significant difference between the RI and serum creatinine levels at different time intervals (0. 72±0.04; P<0). A strong significant connection was found between the RI and serum creatinine (t = 0. 418; p = 0.001). Regarding blood urea, our findings were similar to those of Raut et al: blood urea levels increased by 49. 8422 mg/dl and were found to have a significant connection with renal resistance index (p = 0.001). [17]

In the current analysis, microalbuminuria was found to be 28.578%. Ishimura et al found that RI measurements in group 4 were significantly higher than those in groups I, II, and III (p0.0001).(22) The difference between groups without albuminuria (mean RI 0.67), microalbuminuria (mean RI 0 .71) and macroalbuminuria (mean RI 0.71) was statistically significant (p0.001), according to Fallah et al.[7]

According to Ghadirpour et al. there was a progressive rise in RI values as urinary albumin increased.[18] The results of the current study were consistent with their previous research. Raut et al., found a statistically significant association between RI and microalbuminuria ($p<0.001$).[17]

However, when examining the results of this analysis, the proposed relationship between HbA1c and RI was not found to exist (p=0. 217). In agreement with Ljubic et al, Thukral et al, and Ishimura et al, the results revealed that the correlation between HbA1c and RI was not statistically significant and had a p value greater than 0. 005. It was noted that there was no significant difference regarding the Gender, Age, BMI, DM 2 duration and HbA1c between the two groups (table 1) $p > 0.05$.[21]

No association was found between 24-hour protein and renal resistance index, as reported by Afsar et al., simulating the results of the current study.[11] The researchers found a positive correlation between RI and 24-hour urinary albumin.[22]

Spomenka et al. discovered that Doppler imaging can be used to detect diabetic nephropathy earlier via the measurement of intrarenal arterial RI. They also discovered a substantial positive association between intrarenal RI and diabetic nephropathy, which is in line with our findings.[22] Nejad et al. revealed that RI may be employed to evaluate 24-hour urine protein, especially in individuals who lack the ability to provide 24-hour urine.[23] Previous studies demonstrated a link across RI and serum creatinine among individuals with microalbuminuria. Soldo et al. discovered a correlation between RI and serum creatinine.[24] Our investigation found outcomes similar to earlier studies in patients with increased serum creatinine levels (3.97±0.70).[25] Elevated HbA1c is thought to be a separate risk component for cardiovascular disease including stroke, whether or not the patient has diabetes. Just one HbA1c test is a reliable biomarker for diagnosing and treating diabetes.[26] According to a newly published study, the association value across HbA1c and resistance index is 0.162, demonstrating that as HbA1c levels rise, so does the resistance index. The association is positive, with a p-value of 0.217. This suggests that an elevated HbA1c level suggested kidney pathology or diabetes. Elevated HbA1c levels have been established as a major risk indicator for cardiovascular disease and stroke in individuals with diabetes.[27]

One important limiting factor of this was that it was conducted during pandemic COVID-19 due to which the change in the RI over time was not assessed.

CONCLUSION

As a result, we found that the renal artery resistivity index, calculated via duplex Doppler ultrasonography, constitutes a noninvasive procedure that may be related with biochemical indicators of renal impairment in type 2 diabetic (DM2) individuals who have kidney failure due to diabetes. Using RRI we can prevent progression of diabetic nephropathy at early stages and also there will be reduced risk of blood born infections or diseases by avoiding needle pricking during blood sampling.

CONFLICT OF INTEREST / DISCLOSURE: Nil.

FUNDING SOURCE: Nil.

AUTHORS' CONTRIBUTION:

MN: Acquisition of data, manuscript writing, statistical analysis and data interpretation final approval of manuscript.

SM: Acquisition of data, data analysis and interpretation,

SAQ: Conceived, designed and manuscript writing, Statistical analysis and data interpretation final approval of manuscript.

MF: Data analysis and interpretation, manuscript writing

REFERENCES

1. Ljubiæ S, Brkljaèiæ B, Metelko Z, Renar IP. Renal resistance index in type 2 diabetes. Diabetologia Croatica. 2006; 35 (1):7-13.
2. Milovanceva-popovska M, Dzikova S. progression of diabetic nephropathy: value of intrarenal resistive index. Prilozi. 2007; 28(1): 69-79.
3. Malik A. Diabetes Prevalence Data in Pakistan: survey, The News International. 2017. [Accessed: 5-7-2019]
4. Thukral C, Aggarwal M, Nayyar S. Intrarenal haemodynamic in type 2 diabetes mellitus and its correlation with biochemical parameters. Journal of evolution of medical and dental sciences. 2015; 4(37):6384-9.
5. Padman A, Jacob V, Retnakumari V. Role of renal Doppler in early detection of diabetic nephropathy. Journal of Evolution of Medical and Dental Sciences. 2013; 2(52) :10270-6.
6. Moghazi S, Jones E, Schroepple J, Arya K, Mcclellan W, Hennigar RA, et al. Correlation of renal histopathology with sonographic findings. Kidney International. 2005; 67(4): 1515-1520.
7. Fallah M, Nafisi-Moghadam R. Relationship between Intrarenal Arterial Resistance Index (RI) and Albuminuria in Diabetic Patients. 2012;4(1):7-10.
8. Maja M-P, Sonja D. The value of intrarenal resistive index in diabetic nephropathy. Bantao Journal. 2009;7(1):38-44.
9. Nosadini R, Velussi M, Brocco E, Abaterusso C, Carraro A, Piarulli F, et al., Increased renal arterial resistance predicts the course of renal function in type 2 diabetes with microalbuminuria. Diabetes. 2006; 55(1):234-9.
10. Viazzi F, Leoncini G, Derchi LE, Pontremoli R. Ultrasound Doppler renal resistive index: a useful tool for the management of the hypertensive patient. Journal of hypertension. 2014 ;32(1):149.

11. Afsar B, Elsurer R. complications comparison of renal resistive index among patients with type 2 diabetes with different levels of creatinine clearance and urinary albumin excretion. Diabet. Med. 2012;29: 1043-46
12. Masulli M, Mancini M, Liuzzi R, Daniele S, Mainenti PP, Vergara E et al., Prediction of diabetic nephropathy. Nutr dis. 2009;19(5): 358-364.
13. Zwain AA. Intrarenal hemodynamic changes in type 2 diabetic patients. Kufa medical journal. 2010;13(1):205-13.
14. Sari A, Dinc H, Zibandeh A, Telatar M, Gümele HR. Value of resistive index in patients with clinical diabetic nephropathy. Invest Radiol 1999; 34(11): 718-21.
15. Vedaraju K, Benegal DS. Correlation of Renal Artery Resistive Index with Albuminuria and Other Risk Factors in Type 2 Diabetes Mellitus Patients. International Journal of Contemporary Medicine Surgery and Radiology. 2019; 4(1):A65-A68.
16. Kaya M. The evaluation of renal hemodynamics with Doppler ultrasonography. Hemodynamics-New Diagnostic and Therapeutic Approaches. 2012; 25:1-31.
17. Raut TP, Patil TB, Khot RS, Sargar KM, Patil MB, Bansod YV. Clinical profile of diabetic nephropathy and correlation with intrarenal resistivity index by duplex ultrasonography. World Journal of Nephrology and Urology. 2012;1(4-5):107-14.
18. Ghadirpour A, Tarzamni MK, Naghavi-Behzad M, Abedi-Azar S, Koushavar H, Nezami N. Renal vascular Doppler ultrasonographic indices and carotid artery intima-media thickness in diabetic nephropathy. Medical ultrasonography. 2014;16(2):95-9.
19. Shirin M, Sharif MM, Gurung A, Datta A. Resistive index of intrarenal artery in evaluation of diabetic nephropathy. Bangladesh Medical Research Council Bulletin. 2015;41: 125-130.
20. Platt JF, Rubin JM, Ellis JH, Diabetic nephropathy: evaluation with renal duplex Doppler ultrasonography. Radiology. 1994; 190(2): 343-346
21. Genov D, Kundurdgiev A, Pencheva V. Resistive Index for the Evaluation of Renal Damage in Diabetes Mellitus Type 2. Open Journal of Internal Medicine. 2018; 8(02):160.
22. Ishimura E, Nishizawa Y, Kawagishi T, Okuno Y, Kogawa K, Fukumoto S, et al., Intrarenal hemodynamic abnormalities in diabetic nephropathy measured by duplex Doppler sonography. Kidney international. 1997;51: 1920-27.
23. Spomenka LJ, Boris BR, Ivana PA. Renal resistance index in type 2 diabetes. Diabetologia Croatica. 2006; 35(1): 1-35.
24. Nejad MN. Arterial Resistive Index (RI) in Type II Diabetic Nephropathy Stages and Healthy Controls. Iranian Journal of Radiology, 2009;6(1): 29.
25. Soldo D, Brkljacic B, Bozikov V, Drinkovic I, Hauser M. Diabetic nephropathy. Comparison of conventional and duplex Doppler ultrasonographic findings. Acta Radiologica. 1997;38(2): 296-302.
26. Sherwani SI, Khan HA, Ekhzaimy A, Masood A, Sakharkar MK. Significance of HbA1c test in diagnosis and prognosis of diabetic patients. Biomarker insights. 2016 Jan;11:BMI-S38440.
27. Martin-Timon I, Sevillano-Collantes C, Segura-Galindo A, del Cañizo-Gómez FJ. Type 2 diabetes and cardiovascular disease: have all risk factors the same strength? World J Diabetes. 2014;5:444–70.