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# A COMPARATIVE STUDY TO EVALUATE THE ROLE OF RENAL DOPPLER AND SHEAR WAVE ELASTOGRAPHY IN DIABETIC NEPHROPATHY

**Radio-Diagnosis**

**Hari Prasad** Junior Resident, Department of Radiodiagnosis, SMS Medical College, Jaipur, Rajasthan, India.

**Ayush Gupta*** Junior Resident, Department of Radiodiagnosis, SMS Medical College, Jaipur, Rajasthan, India. *Corresponding Author

**Manit Kulariya** Junior Resident, Department of Radiodiagnosis, SMS Medical College, Jaipur, Rajasthan, India.

**Pragya Surolia** Assistant Professor, Department of Radiodiagnosis, SMS Medical College, Jaipur, Rajasthan, India.

## ABSTRACT

**Introduction:** Diabetic nephropathy is most common cause of chronic kidney disease. Grey scale ultrasound is commonly used to see renal cortical echogenicity, size and corticomedullary differentiation. Color doppler and shear wave elastography (SWE) are newer, non invasive imaging methods for early diagnosis of diabetic nephropathy. **Aim:** To evaluate the changes in the resistive index (RI) of intrarenal segmental arteries and shear wave modulus in diabetic nephropathy cases and controls with correlation of the findings with stages of diabetic nephropathy. **Material and methods:** An observational study was carried out at tertiary care hospital using ultrasound scanner Samsung HS70A with color doppler and shear wave elastography capability. Total 100 subjects were included in the study after taking informed consent and approval from ethical committee of institution. Total 50 patients with history of Type 2 diabetes mellitus and another 50 patients presenting to the department of radiology for ultrasound with normal serum creatinine and blood sugar were included as controls. Color doppler and SWE were done in each patient for both kidneys. The mean RI and shear modulus for each stage of diabetic nephropathy was obtained. The mean RI and shear modulus values for each stage of diabetic nephropathy were compared separately with controls. **Result:** The mean RI and shear modulus of the kidneys was $0.72 \pm 0.04$ and $8.68 \pm 1.93$ kPa for the cases. A statistically significant difference was found between RI and shear modulus of each stage of diabetic nephropathy as compared to controls. Between the control group and the cases cut off value of 0.650 for RI and 5.310 kPa for shear modulus gave maximum accuracy. **Conclusion** : The mean RI of the kidneys increases in diabetic nephropathy and progressive increase in RI with the stage of diabetic nephropathy is also noted. The shear modulus of the kidneys also increases in diabetic nephropathy. The rise is marked in the early stages and then decreases in advanced stages. Combination of renal Doppler and shear wave elastography can be used for the early diagnosis of diabetic nephropathy.

## KEYWORDS

Diabetic nephropathy, Color Doppler, Shear wave elastography, Resistive index.

## INTRODUCTION

Diabetes mellitus is the most common cause of chronic kidney disease (CKD) in India. [1] The prevalence of diabetic nephropathy in Indians with Type 2 Diabetes Mellitus based on various studies is 5 – 9 %. [2,3,4] It is usually diagnosed by micro albuminuria and progressive reduction in GFR. Micro albuminuria is defined as 30 to 300 mg of albumin in 24 hours urine is usually not detected by conventional methods. [5] The sensitivity and specificity of micro albuminuria for the early diagnosis of diabetic nephropathy is low. [6,7]

Most commonly used imaging modality for the kidneys in diabetic nephropathy is grey scale ultrasonography (USG). Renal ultrasound is useful to see echogenicity, cortico-medullary differentiation (CMD) and to measure kidney size. In CKD, the kidney size reduces progressively. [8] However grey-scale ultrasound changes appear late in the disease so it is not useful in early diagnosis or follow-up. [9] Colour doppler sonography can detect changes in renal volume and hemodynamics in diabetic patients without proteinuria and with both normal and increased glomerular filtration rates. So duplex sonography can be used in the early diagnosis of diabetic nephropathy. [10]

Shear wave elastography (SWE) is a newer imaging modality which measures the tissue elasticity by using acoustic radiation force to transiently deform tissues in the region of interest. [11] SWE can be used in early diagnosis of diabetic nephropathy by quantitative measurement of elasticity changes occurring in the kidney due to disease.

This study was done to show role of both color doppler and shear wave elastography in diagnosing diabetic nephropathy specially in early stages.

## MATERIALS AND METHODS

An observational study was carried out at tertiary care hospital from April 2021 to September 2022 using ultrasound scanner Samsung HS70A (2- 5 MHz convex transducer) with color doppler and shear wave elastography capability. Total 100 subjects were included in the study after taking informed consent and approval from ethical committee of institution. Total 50 patients with history of Type 2 diabetes mellitus for more than 5 years were included as patients and another 50 patients presenting to the department of radiology for ultrasound with normal serum creatinine, blood sugar and not suffering from any condition affecting the kidney were included as controls. Obese patients, hypertensive patients with long standing hypertension > 5 yrs prior to detection of diabetes, patients with obstructive uropathy and coexistent renal diseases or anomalies were excluded from study.

For all cases the age, sex, duration of diabetes, history and duration of hypertension were noted and current blood pressure was recorded. For all controls the age, sex and blood pressure were recorded. Only normotensive subjects were chosen. Grey scale ultrasound was performed in each patient for both kidneys. Both kidneys were assessed for renal size, shape, position, echogenicity and presence of any calculi, hydronephrosis or any features which exclude the subject from the study. Color doppler was done in each patient for both kidneys. The segmental arteries were identified and six waveforms from the arteries of the upper, middle and lower poles of each kidney were obtained. Average Resistive Index (RI) for both kidneys was calculated.

Shear wave elastography was performed in each patient for both kidneys. The Region of Interest (ROI) cursor was placed over 3 cortical regions of each kidney and at least 2 measurements were taken from each region. Renal sinuses and capsules were excluded. Mean of quantitative values for both kidneys were calculated.

Statistical analysis: The mean resistive index and shear modulus for each stage of diabetic nephropathy was obtained. The resistive index and shear modulus values for each stage of diabetic nephropathy were compared separately with the values for the controls using student t tests and p values obtained for significance. The differences in shear wave values and resistive index between controls and cases in five different stages of diabetic nephropathy were analyzed using one way ANOVA tests and p values were obtained. p value $<0.001$ was considered statistically significant.

The statistical measures of performance of resistive index and shear modulus were assessed by calculating the sensitivity, specificity, positive predictive value, negative predictive value, positive likelihood ratio and negative likelihood ratio for various cut offs of resistive index and shear modulus. Cut off value with highest accuracy was identified and receiver operating characteristic (ROC) curves was generated.

## RESULTS

A total of 50 controls and 50 patients with diabetic nephropathy (cases) were included in the study. Among the controls and cases the mean age was 43.32 ± 9.11 years and 55.12 ± 8.51 years respectively.

**Controls**: The mean resistive index (RI) of the kidneys was 0.62 ± 0.04 in the controls. The mean shear modulus of the kidneys for the controls was 4.46 ± 0.57 kPa. A progressive increase in the resistive index as well as the shear modulus of the kidneys was found in the controls with increase in age and this was statistically significant ($p < 0.001$).

**Cases:** The mean resistive index of the kidneys was 0.72 ± 0.04 in the cases. The mean shear modulus of the kidneys for the cases was 8.68 ± 1.93 kPa. For each case, the estimated GFR calculated from the serum creatinine value using the modified MDRD equation. Then cases were divided into chronic kidney disease stages I to V based on the eGFR values. The resistive index as well as the shear modulus of the cases were also found to statistically significantly correlate with the stage of diabetic nephropathy based on the eGFR value ($p < 0.001$).

### Cases Versus Controls:

**Resistive Index:** The mean resistive index of the cases for each stage of diabetic nephropathy is tabulated in Table/Fig 1. A statistically significant difference was found between the resistive index of each stage of diabetic nephropathy as compared to the controls ($p < 0.001$).

**Shear Modulus:** The mean shear modulus of the cases for each stage of diabetic nephropathy is tabulated in Table/Fig 2. A statistically significant difference was found between the shear modulus of each stage of diabetic nephropathy as compared to the controls ($p < 0.001$).

**Statistical Measures Of Performance:** Between the control group and the cases, 0.650 a cut off value of the resistive index of both kidneys gave maximum accuracy of 0.831 for the diagnosis of diabetic nephropathy. The results are tabulated in Table/Fig 3. The AUC value for the ROC curve was 0.916 ($p < 0.001$, $\alpha$ of 0.05). Between the control and cases with diabetic nephropathy, 5.310 kPa a cut off value of the shear modulus of both kidneys gave maximum accuracy of 0.877 for the diagnosis of diabetic nephropathy. The results are tabulated in Table/Fig 4. The AUC value for the ROC curve was 0.923 ($p < 0.001$, $\alpha$ of 0.05). Case in stage two diabetic nephropathy showing values of RI and shear modulus above cut off is shown in Table/Fig 5.

**Combined RI and SWE for diagnosis of diabetic nephropathy:** When the tests are combined in "and" manner, overall sensitivity was 0.817 and overall specificity was 0.963. Overall accuracy was 0.890. When the tests are combined in "or" manner, overall sensitivity was 0.990 and overall specificity was 0.645. Overall accuracy was 0.818.

## DISCUSSION

The study was done to detect the changes in the intrarenal resistive index and elasticity of the renal parenchyma measured by shear modulus in diabetic nephropathy. Diabetic nephropathy was diagnosed by microalbuminuria and then divided into stage I to stage V on the basis of eGFR.

In controls the mean resistive index of the intrarenal arteries was slightly higher for females (0.63) than that of males (0.62). However, the difference was not statistically significant. Shear modulus of the kidneys was also slightly higher for the males (4.48 kPa) than the females (4.43 kPa). However, the difference was not statistically significant. This is consistent with other studies which have shown that there is no significant variation of intrarenal resistive index or shear modulus with sex. [12,13]

A significant increase in the resistive index was found with increase in the age of the patient. All subjects above 60 years of age in the study showed RI of > 0.65. This concurs with the findings of previous studies that age is a significant factor influencing intrarenal resistive index and could act as a confounding factor. [12, 14] Shear modulus also showed a significant increase with increase in the age of the patient. Some studies have found no significant correlation of shear modulus with age while other studies have found results similar to this study. [15,16,17]

The mean resistive index of the cases (0.72) was found to be significantly higher than the mean resistive index of the controls (0.62). A progressive increase in the mean intrarenal resistive index was found with each stage of diabetic nephropathy, with the highest values in Stage V of diabetic nephropathy (mean of 0.79). This is due to endothelial dysfunction and progressive vascular injury in the diabetic kidneys resulting into elevation in RI as discussed previously. [18,19,20]

The mean shear modulus of cases (8.68 kPa) was also significantly higher than the mean shear modulus of the controls (4.46 kPa). A significant difference in the shear modulus was noted in each stage of diabetic nephropathy compared to the controls. The shear modulus showed significant increase in the early stages of diabetic nephropathy, with highest values in the Stage II (11.38 kPa). The mean shear modulus of kidneys in Stage I diabetic nephropathy (9.06 kPa) was also double the mean shear modulus of controls (4.46 kPa) showing its role as a sensitive diagnostic tool. The rise in shear modulus in the early stages (Stage I and II) of diabetic nephropathy is due to glomerular and tubular hypertrohy. In the later stages (Stage III to V) the reduced function of kidneys and progressive glomerulosclerosis results in progressive decrease in shear modulus. Similar observations have been made by Goya et al. in their study. [13] These findings showed SWE can be used in the diagnosis of early stages of diabetic nephropathy.

When the two tests were combined for diagnosis of diabetic nephropathy, if positive results in both tests was taken as diagnostic, the sensitivity was lower than for either test alone (0.817) but the specificity was much higher (0.963). However, the overall accuracy was higher than either test alone (0.890).

**Limitation:** The age group of the controls and cases was also different, with majority of controls in the 31 – 40 years and 41 – 50 years age and majority of the cases in the 51 – 60 years age . There were no cases in the 21 – 30 years age group while few controls were selected from this age group. As a statistically significant difference in resistive index as well as shear modulus was found with age among the controls, a possible source of error exists due to the unequal age distribution of the controls and cases.

## CONCLUSION:

The intrarenal resistive index of the kidneys increases in patients with diabetic nephropathy and progressive increase in resistive index with the stage of diabetic nephropathy is also noted. The shear modulus of the kidneys also increases in patients with diabetic nephropathy. The rise is marked in the early stages and then decreases in advanced stages of diabetic nephropathy. Combination of renal Doppler and shear wave elastography can be simple, noninvasive, inexpensive and accurate tool for the early diagnosis of diabetic nephropathy.

**Table/Fig 1. Mean resistive index of the controls and cases for each stage of diabetic nephropathy**

| STAGE OF CKD | RESISTIVE INDEX (Mean ± SD) | RANGE |
|---|---|---|
| Normal | 0.62 ± 0.04 | 0.54 – 0.72 |
| I | 0.67 ± 0.02 | 0.63 – 0.71 |
| II | 0.70 ± 0.02 | 0.64 – 0.75 |
| III | 0.71 ± 0.03 | 0.65 – 0.76 |
| IV | 0.75 ± 0.03 | 0.68 – 0.79 |
| V | 0.79 ± 0.01 | 0.77 – 0.82 |

**Table/Fig 2. The mean shear modulus of the controls and cases for each stage of diabetic nephropathy**

| Stage of CKD | Shear Modulus (Mean ± SD) (kPa) | Range |
|---|---|---|
| Normal | 4.46 ± 0.57 | 3.57 – 6.45 |
| I | 9.06 ± 0.68 | 7.96 – 10.35 |
| II | 11.38 ± 0.97 | 9.82– 12.85 |
| III | 8.35 ± 0.33 | 7.84 – 9.13 |
| IV | 7.19 ± 1.10 | 4.56 – 8.38 |
| V | 5.60 ± 0.48 | 4.86 – 6.23 |

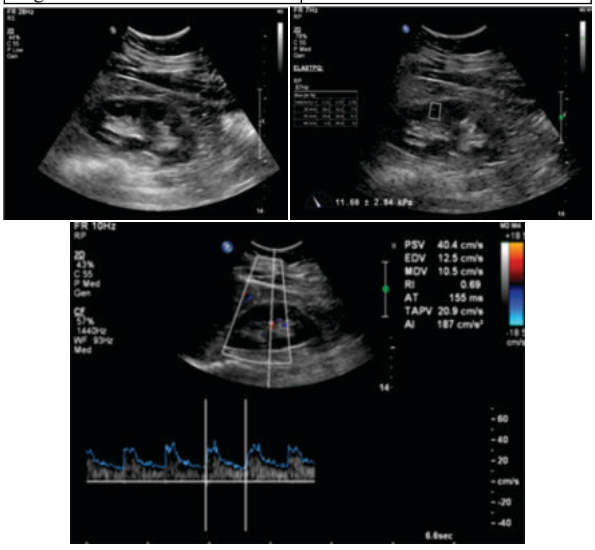
**Table /Fig 3. Statistical measures of performance for resistive index at cut off of 0.650**

| | |
|---|---|
| Accuracy | 0.831 |
| Sensitivity | 0.900 |
| Specificity | 0.762 |

| | |
|---|---|
| Positive Predictive Value | 0.791 |
| Negative Predictive Value | 0.884 |
| Positive Likelihood Ratio | 3.774 |
| Negative Likelihood Ratio | 0.131 |

**Table/Fig 4. Statistical measures of performance for shear modulus at cut off of 5.310 kPa**

| | |
|---|---|
| Accuracy | 0.877 |
| Sensitivity | 0.908 |
| Specificity | 0.846 |
| Positive Predictive Value | 0.855 |
| Negative Predictive Value | 0.902 |
| Positive Likelihood Ratio | 5.900 |
| Negative Likelihood Ratio | 0.109 |




**Table/Fig 5**. Grey mode ultrasound of a patient with Stage II diabetic nephropathy shows no increase in cortical echogenicity. Corticomedullary differentiation is well maintained. Shear wave elastography of the same patient shows cortical shear modulus of 11.60 ± 2.84 kPa reading. The mean shear modulus of the kidneys for this patient was 11.43 kPa, which is much higher than the cut off value of 5.310 kPa for diagnosis of diabetic nephropathy. Renal Doppler of the same patient shows resistive index of 0.69. The mean intrarenal resistive index of the kidneys was 0.71 which is higher than the cut off value of 0.650 for the diagnosis of diabetic nephropathy.

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