ROLE OF RENAL DOPPLER IN EARLY DETECTION OF DIABETIC NEPHROPATHY

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ABSTRACT: The RI (Resistive Index) changes in renal inter lobar segmental arteries were studied in fifty diabetic patients and other 35 random cases. 98% of documented cases of diabetic nephropathy showed raised RI values, more than 0.7. The RI value of one diabetic nephropathy case (2% of cases) was only 0.68. Another one case showed raised RI values, even when the urine microalbuminuria level was only the upper normal value (30mg/L). This shows that renal interlobar segmental artery Doppler evaluation is as sensitive as the urine microalbuminuria study to detect the diabetic renal involvement, and rarely the Doppler study is seen to have an edge over the urine microalbuminuria assessment.

KEYWORDS: Renal Doppler, Resistive Index, Diabetic Nephropathy, microalbuminuria, NIDDM

AIM & OBJECTIVES: In this study our aim was to

- Find the sensitivity of Doppler to detect diabetic nephropathy
- Find out the positive predictive value for diabetic nephropathy by renal doppler
- And whether it can be used as a safe, reliable, non-invasive procedure to detect diabetic renal involvement

RESULTS: The results of our study were as follows

- NIDDM with raised RI was found in 39 cases (78%)
- Previously documented cases of diabetic nephropathy was seen in 30 cases (76%)
- Newly detected diabetic renal involvement cases by the Doppler 9 cases (23%)
- Cases with raised RI values but normal urine microalbumin at the time of Doppler, and thereafter who developed microalbuminuria after 4 months, were: 4 (10%).

CONCLUSION: In our study the renal inter lobar artery, RI evaluation is a sensitive test of diabetic nephropathy and in a few cases it is more sensitive than urine microalbumin level. So cases with raised RI values in serial studies have some prognostic predictive value for future renal involvement.

INTRODUCTION: For many years Doppler evaluation has been routinely done to detect renal artery stenosis in patients presenting with severe uncontrolled secondary hypertension. In the last decade, it has been found that renal Doppler can be effectively used to check the renal bed defects also. Most of the renal involvement of systemic diseases, mainly affect the glomeruli. So by assessing the renal glomeruli changes it is possible to quantify renal damage. One of the methods of assessing the renal glomeruli is by biopsy. However biopsy is an invasive procedure and at times lead to fatal complications. Another option of studying the renal glomeruli is by Doppler evaluation. It is possible to assess the renal glomeruli changes by measuring the Doppler indices in renal inter

lobar segmental arteries. As the glomeruli are the distal capillary bed in kidneys, all the changes occurring there will produce changes in Doppler indices of proximal inter lobar segmental arteries.

Studies have shown that RI values in segmental arteries is a good indicator of changes in the distal glomeruli. In non-insulin dependent diabetes mellitus, the renal involvement is mainly due to glomerular sclerosis, and mesangial thickening. The glomerular capillary changes will produce an increase in RI in renal segmental arteries. Multiple studies^{1,2} in diabetic patients have been seen to be supporting our finding.

Many studies³⁻⁵ have shown that the cut off level of RI can be taken as 0.7, so RI more than 0.7 is considered as abnormal.

MATERIALS AND METHODS: The study was done in Sree Gokulum Medical College, and Research Foundation in Trivandrum. The total number of patients were 85 of age >30 years. The study was carried out from July 2012, to August 2013.

Serial Doppler study was carried out using GE (Voluson-730 pro) and Toshiba Nemio XG machines with 3.5 MHz probes.

Cases with obstructive uropathy and infections causing acute renal failure were excluded from the study. The number of known NIDDM cases were 50 and non-diabetic and non-renal cases which were used as control group was 26. The number of cases, of nephropathy due to diseases other than Diabetes mellitus, and with borderline RI values, was 9.

DISCUSSION: The renal change that primarily happens in long standing diabetic mellitus is mainly due to the vascular changes. The diabetic renal involvement is mainly classified into five stages:

Stage 1: Hyper Filtration stage

In this stage the GFR increases. No pathological signs will be seen in mesangium or capillary bed

Stage 2: Stage of mesangial thickening

The GFR becomes normal. No microalbuminuria or vascular changes will be seen in this stage

Stage 3: Stage of microalbuminuria

In this stage glomerular (capillary) changes occur. The main pathology is glomerular sclerosis. Microalbuminuria occurs in this stage. The Doppler changes also start in this stage.

Stage 4: Stage of proteinuria

In this stage gross glomerular defects are already formed and gross proteinuria will be present. Definite Doppler changes will be present in this stage.

Stage 5: Stage of end stage renal dysfunction

In this stage overt dysfunction of kidneys occurs. The serum creatinine level rises. Definite changes will be seen in Doppler studies

Among these five stages, up to 3rd Stage (Stage of microalbuminuria) is considered as reversible. The 4th and 5th stages are irreversible.

The microalbuminuria starts in the early stages of glomerular sclerosis. The Doppler changes also start in this stage of glomerular sclerosis. The significance of the Doppler evaluation is in this stage. Microalbuminuria and Doppler changes start in the same Stage. We can conclude therefore that early detection of diabetic renal involvement is possible with renal Doppler evaluation. These findings aligned to the study done by Argalia G, D' Ambrosio F, Mignosi U, Migliorini D, Lucarelli F,

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Giuseppetti GM, Fanciulli E, Mioli V ⁶, in Doppler echography and color Doppler echography in the assessment of the vascular functional aspects of medical nephropathies.

Fig. 1: Majority of the cases are seen between the ranges of 0.72 to 0.81, for known diabetic cases

Fig. 2: RI values for non-diabetic cases are lesser and peak between 0.63 to 0.71

Fig. 3: Diabetic Distribution of PI ranges from 1.4 to 2.1

Fig. 4: PI values for non-diabetic cases are lesser and peaky between 1.00 to 1.30

In our study of a total of 85 patients, at least one inter lobar segmental artery of either kidney was studied. The PI and RI values of these vessels were measured and documented. RI of more than 0.7 was taken as abnormal. (Figures 1 -4)

- In our study of 85 cases, the total number of NIDDM cases: 50
 - Diabetic patients showing raised RI (>0.7): 39
 - Previously documented cases of renal involvement: 30
 - Newly detected diabetic renal involvement cases by the present Doppler study: 9
- Of these 9 cases the following was the sub distribution:
- 6 cases do not possess any bio chemical supporting results, like urine microalbuminuria levels, urine albumin levels or serum creatinine levels.
 - 2 cases show raised RI values but the urine albuminuria levels within normal ranges. Out of these 2 cases, one case is a known hypertensive patient, and systemic hypertension is also known to cause raised RI values in the renal inter lobar arteries.

- The other case was a known diabetic for 3 years, not hypertensive and does not have any other renal diseases. The microalbuminuria is 30 mg/L, which is the upper normal level. This was slowly crossing to the abnormal side, at which time the Doppler was showing raised RI value, RI – 0.78). This proves that at least in some cases Doppler evaluation is having slightly increased sensitivity as compared to the urine microalbuminuria assessment. Both changes that is, increased urine microalbuminuria and Doppler changes occur in the same phase of diabetic nephropathy. From our study we assume that at least in some cases, it may take some more time for the urine microalbuminuria to increase to abnormal levels. By this time there will be changes in Doppler measurements. Urine microalbuminuria is a functional defect that may be delayed for some time in certain patients. However, renal Doppler on the other side measures the primary changes that happen to the glomeruli capillary band and has an edge over the functional changes.

The normal range of RI value seen in adult is between 0.60 and 0.70 (Figure 2). The values of 0.60 to 0.70 may be considered as borderline values. RI of more than 0.70 was considered to be elevated RI as seen in Figure 2. So it is accepted that a reasonable cut off value for RI is 0.70. However all cases with RI values between 0.64 and 0.70 should be viewed with suspicion and needs to be followed up (Figures 5 – 8). The studies by Brkljacic B, Mrzlkak V, Drinkovic I, Soldo D, Sabljari – Matovinovic M, Hebrang A ⁷, and Derch LE, Martinoli C, Saffioti S, Pontremoli R, De Micheli A, Bordone C ⁸ share this assessment.

Ultrasonographic Imaging and Doppler analysis of renal changes in non-insulin dependent diabetes mellitus were seen to have similar findings.

Fig 5: Doppler of upper pole inter segmental artery of right kidney showing raised RI value of - 0.72

Fig 6: Doppler of mid pole inter segmental artery of right kidney showing raised RI value of - 0.72

Fig. 7: Doppler of mid pole intersegmental artery of left kidney showing raised RI value of - 0.74

Fig. 8: Doppler of lower pole intersegmental artery of left kidney showing raised RI value of - 0.74

Another observation that was made was as age increases, there was a tendency for increasing RI values. This could be due to generalized vascular changes like arterio sclerosis that happens as age progresses. The finding was corroborated by the study on age dependence of renal RI in healthy children by Bude RO, DiPietro MA, Platt JF, Rubin JM, Miesiewicz S, Ludquist C⁹

One case with impaired glucose tolerance test but without documented diabetes mellitus or hypertension had an RI value of 0.69. The patient was a chronic alcoholic with cirrhosis of liver. This marginal increase in RI value could be due to alcohol intake and post cirrhotic biochemical changes. As blood glucose levels were not severely increased in this patient. NIDDM may not be the cause for this marginal RI value increase.

7 other cases that are not diabetic also show raised RI levels of more than 0.70. These cases were classified according to the disease such as

- Long standing systemic Hypertension – 2 cases
- Obstructive uropathy – 1 case
- Metabolic disease like hyper uricaemia – 1 case
- Hyperlipidaemia – 1 case

All of these conditions are also known to cause increase in RI. As RI values are just reflection of the glomeruli capillary changes, any condition that causes capillary bed damage will also show RI changes.

CONCLUSION: Of 50 diabetic patients, 39 had an RI value of more than 0.70. Of these 39 cases, 30 cases were known diabetic nephropathy cases. 9 cases were not known diabetic nephropathy cases and only the present Doppler evaluation showed renal involvement. All known cases of diabetic renal involvement showed RI values of > 0.70. It was seen that 98% of the cases with known diabetic renal involvement (cases with raised urine microalbuminuria/ protein urea/serum creatinine levels according to the stage of nephropathy) were picked up as positive cases in renal segmental artery Doppler evaluation.

One case with upper normal level of urine, microalbuminuria (30 mg/L) showed increased RI value of 0.78 which means that, in certain cases Doppler has an edge over urine microalbuminuria evaluation; this is probably due to mild delay in the functional change to happen. The conclusion of

the above study is renal segmental artery RI evaluation is a sensitive test of diabetic renal involvement and in a few cases a few patients the Doppler changes preceded the elevated urine microalbuminuria levels, the raising RI value in renal segmental artery, directly gives an idea about the gradual deterioration of capillary bed health. So patients with raising RI values in serial studies have some predictive value for future renal involvement and should be thoroughly followed up.

The final conclusion of this study is that renal Doppler evaluation is a very sensitive test to detect micro-angiopathic changes. Many conditions other than diabetes mellitus also can cause raised RI values, such as hypertension, obstructive uropathy as seen in the study by Ellenbogn PH, Scheible W, Talner LB, Leopold GR ¹⁰ and Gottlieb RH, Luhmann K, Oates RP ¹¹ Duplex ultrasound evaluation of normal native kidneys with urinary tract obstruction, renal vein thrombosis, and metabolic disorders, so the specificity of this investigation is not too high but the sensitivity is as high 98%. Hence, renal Doppler can be used as a good screening modality to detect early renal involvement ¹². At least one renal inter lobar segmental artery should be evaluated in all diabetic patients as routine screening study to detect early diabetic nephropathy.

Also serial Doppler evaluations should be done in specific time intervals and in all long standing diabetic patients, with RI < 0.70, so that the raising RI values in serial studies will positively give a prognostic predictive value for future renal involvement.

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