

**Original article:**

## **Role of renal resistive index in unilateral acute renal obstruction, diabetic and hypertensive nephropathy**

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**Abstract:**

**Background:** Variation in Renal resistive index (RI) values measured using duplex Doppler ultrasonography has been shown to correlate with the degree of renal impairment in acute renal obstruction ,diabetic and hypertensive nephropathy patients.

**Aims and objectives:** The primary objective of this study was to determine whether the intrarenal resistive index can be used as a predictor of progression of disease in patients with unilateral acute renal obstruction and chronic medical renal diseases,especially diabetic and hypertensive nephropathies.We investigated the role of RI in unilateral acute renal obstruction , Diabetic and Hypertensive patients.

**Methodology:** A total of 120 patients were included in this study. 50 patients with unilateral acute renal obstruction , 35 each of diabetic and hypertensive patients. Renal segmental arterial RI was measured by duplex Doppler ultrasonography.

**Results and conclusion:** Regarding renal function outcome,the RI values are relatively high in complete and proximal obstruction by renal calculus compared to distal and partial obstruction. In the case of nephropathies, RI value increase as the duration of the disease progresses and with complications.In conclusion,RI measured using duplex Doppler ultrasonography can be used as an independent predictor of renal function.

**Keywords:** renal resistive index,duplex Doppler ultrasonography.

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**INTRODUCTION:**

Ultrasound and Doppler are noninvasive modalities for evaluation of kidney in various local and systemic diseases. Ultrasound evaluation of kidneys has the additional advantage of being free from ionizing radiation and its possible harmful effects.

Duplex ultrasonography has provided an easily applicable and non-invasive method for investigating renal hemodynamics. Nowadays, a lot of work has been directed towards the use of Doppler in the evaluation of renal vascular resistance by using Doppler indices like the resistive index in various systemic conditions like acute renal obstruction,

Diabetes mellitus, Systemic hypertension, Hemolytic uremic syndrome.

Renal colic (RC) is one of the most common conditions seen in the emergency department (ED). Ranging from 2% to 12% in the general population and it accounts for 30-35% of all urological emergencies. The incidence is higher in men (10-20% Vs 3-5% in women), and 30-40% of all patients experience a symptomatic recurrence within 5 years.<sup>[1]</sup> Obstructive uropathy can be defined as any blockage of urine drainage from the kidney (renal calyces or renal pelvis), ureter, or bladder.<sup>[2]</sup> As a result of the blockage, urine backs up into the

kidneys, causing dilatation of the ureter, renal pelvis, and renal calyces, which can damage the kidney if it is not treated. hydronephrosis is a symptom of obstructive uropathy.<sup>[3]</sup> The most common causes of obstructive uropathy are renal calculi (nephrolithiasis)<sup>[4]</sup>, ureter (ureterolithiasis) or in the urinary tract (urolithiasis).<sup>[5]</sup>

Diabetes mellitus and hypertension are among the most common chronic noncommunicable diseases and are main preventable risk factors for end-stage renal failure, coronary heart diseases and stroke. DM and HTN are collectively known as Syndrome X.<sup>[6]</sup> long term complications of diabetes and hypertension can be divided into macrovascular and microvascular disorders. coronary artery disease, myocardial infarction, congestive heart failure, stroke, and peripheral vascular disease are most common macrovascular complications. microvascular complications of diabetes are retinopathy, nephropathy, and neuropathy.

The primary objective of this study was to determine whether the intra renal resistive index can be used as a predictor of progression of disease in patients with unilateral acute renal obstruction and chronic medical renal diseases, especially diabetic and hypertensive nephropathies.

#### **AIMS AND OBJECTIVES:**

- To evaluate the role of Resistive Index and compare the Doppler waveform alterations in a unilateral acute renal obstruction (UARO) with the contralateral normal kidney as a control.
- To evaluate the role of duplex Doppler renal resistive index as a predictor of progression of nephropathy in chronic medical diseases especially in diabetes mellitus and hypertension.

#### **MATERIALS AND METHODS:**

In this prospective analysis, 120 patients referred from various Departments of Sri Lakshmi Narayana Institute of Medical Sciences And Research, Pondicherry were included (50 patients with unilateral acute renal obstruction, 35 patients each with diabetes mellitus and hypertension). All patients are divided into two groups :

Group 1: patients presenting to the emergency medical division with symptoms of unilateral acute renal colic, out-patients, in-patients admitted with obstructive uropathy

Group 2: patients with diabetes mellitus and hypertension (recently diagnosed-less than 5 years, 5 to 10 years and more than 10 years) presenting with complications of diabetes and hypertension (nephropathies) are selected.

All patients with Unilateral renal calculi causing obstruction, Patients diagnosed with diabetes mellitus and hypertension and Patients in the age group of 20 to 65 years were included.

Patients with bilateral renal calculi, Normal anatomic variants of kidneys and ureter,

Post renal transplant kidney patients, Pregnant females where right sided pelvicalyceal dilatation is a physiologic entity, Patients with bilateral outflow tract obstruction like benign prostatic hyperplasia (BPH), bladder tumors, trauma and congenital anomalies were excluded.

#### **INSTRUMENTATION USED:**

- The procedure is performed with ULTRASONIX SONIX-SP ultrasonography machine.
- A curvilinear probe of 3.5 MHz is recommended together with the use of color or power Doppler to help vessel localization.

- Obstruction was confirmed by intravenous urography or computed tomography scan where ever required.
- Required laboratory investigations – serum creatinine , glycosylated hemoglobin (HbA1c) , random blood sugar and lipid profile (total serum cholesterol).

#### Technique:

As resistance to blood flow progressively increases from the hilar arteries toward the more peripheral parenchymal vessels, it is generally recommended that sampling for Renal Resistive Index should be done at the level of the arcuate or interlobar arteries, adjacent to medullary pyramids. An RRI is calculated with the following formula:

$$\text{RRI} = (\text{peak systolic velocity} - \text{end diastolic velocity}) / \text{peak systolic velocity},$$

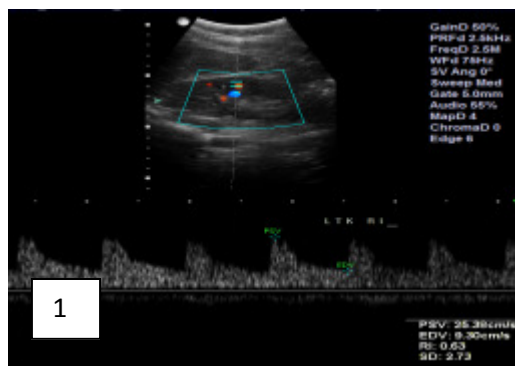


Figure 1 -normal resistive index in 25-year-old healthy man. Color Doppler sonogram is used to identify interlobar artery and waveform is maximized using lowest pulse repetition frequency possible, maximum gain and lowest wall filter.

The mean value of three measurements (superior, median and lower pole) in each kidney is usually considered. An RRI value  $0.60 \pm 0.01$  (mean  $\pm$  SD) is usually taken as normal with a value of 0.70 being considered the upper normal threshold. In order to maximize waveform size, care should be taken in using the lowest pulse repetition frequency without aliasing, the highest possible gain without noise and the lowest wall filter. In children especially within the first year of life [7] and in healthy elderly individuals, the RRI value will be more than the normal limit of 0.7 possibly because of age-related changes in vascular compliance.[8]

Intravenous pyelography (IVP) is considered as the gold standard investigation for confirming the site and degree of renal obstruction.

#### IMAGING AND STATISTICAL ANALYSIS:

Results are expressed as a mean  $\pm$  standard deviation. Categorical variables were presented as number (percentage) and were compared by the or Fisher exact test. The difference between two means was compared by student 't' test for paired /unpaired observations as appropriate. sensitivity and specificity are done by binary classification test.

"p" value of less than 0.05 was accepted as indicating statistical significance.

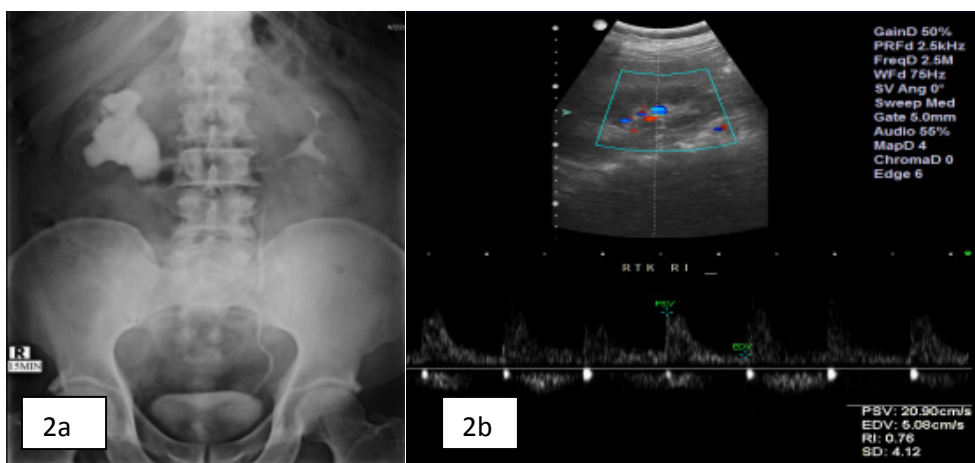
In this analytical study, 120 patients were taken – 50 patients with unilateral acute renal colic, 35 diagnosed cases of diabetes mellitus and 35 diagnosed cases of hypertension. Doppler ultrasound was performed in all cases, intravenous pyelography for patients with renal colic for confirmation of renal calculi and required laboratory investigations like serum creatinine, total cholesterol, glycosylated hemoglobin and microalbuminuria.

First, we will analyse the results in unilateral acute renal obstruction patients. Of 50 patients, 37 are males and 13 are females (sex of the patient was statistically not significant). Most of the patients were evaluated between 4 to 24 hours after the onset of symptoms. resistive index values didn't vary much with duration of onset of symptoms.

Unobstructed contralateral kidneys are taken as controls and let us compare the variation in resistive index value in obstructed and unobstructed control kidneys. The mean resistivity index in obstructed kidneys was significantly higher than in unobstructed kidneys (0.70 Vs 0.61) the difference in R.I ( $\Delta$ R.I)

between obstructed and unobstructed kidney is 0.09. resistive index was higher in all the obstructed kidneys when compared to unobstructed kidneys. Based on the site of obstruction, patients were divided into the proximal obstruction (25 patients) and distal obstruction (25 patients). the  $\Delta$ R.I of the obstructed kidneys with proximal obstruction was higher (0.72), than in the kidneys with distal obstruction (0.66). When compared with contralateral normal kidneys, the  $\Delta$ R.I in proximally obstructed kidneys is higher (0.11) when compared with kidneys with distal obstruction (0.06).

In this study, 16 patients had complete obstruction and 34 patients had a partial obstruction. Resistive index value in completely obstructed kidneys was significantly higher (0.71) than partially obstructed kidneys (0.67). When compared with contralateral normal kidneys, RI was significantly higher even in partially obstructed kidneys. This shows that degree of obstruction was an important parameter affecting the RI value.



**Figure 2(a,b):** 15 min IVP film showing no contrast filling in the right ureter distal to the obstruction indicating complete proximal ureteric obstruction and doppler (2b) shows mean RRI value as 0.76.

Next, we will see the results of chronic medical renal diseases, especially diabetic and hypertensive nephropathy.

A total number of patients involved in this study are 70, of which 35 are diagnosed cases of diabetes mellitus and 35 are diagnosed hypertensives. For all the patient's resistive index is measured and required laboratory investigations like blood pressure, glycosylated hemoglobin, random blood sugar, total serum cholesterol, microalbuminuria, serum creatinine are done.

35 diabetic patients are divided into two groups. Group 1 with RI value  $\geq 0.7$  (25 patients) and group 2 with RI  $\leq 0.7$  (10 patients). All patients were followed up after one year. The resistive index value is correlated with glycosylated hemoglobin and serum creatinine values. Significant increase in the

mean resistive index is noted after 1-year follow-up of patients (0.64 Vs 0.71). The difference in RI ( $\Delta$ RI) was 0.06. Based on the duration of diabetes, all patients are divided into three groups – Group 1 with recently diagnosed diabetes to less than five years, Group 2 with diabetes 5 to 10 years duration and Group 3 with more than 10 years duration. Random blood sugar value is taken into consideration for recently diagnosed patients. HbA1c value and serum creatinine are taken into consideration for Group 2 and Group 3 patients. In group 1 patients  $\Delta$ RI after 1 year of follow-up was 0.06 and rise in serum creatinine ( $\Delta$  s.creatinine) was 1.5 mg/dl. In group 2 patients  $\Delta$ RI was 0.07 and rise in serum creatinine was 1.7 mg/dl. In group 3 patients, duration above 10 years, change in RI was 0.08 (0.65 Vs 0.73) which indicates statistically significant in our study.

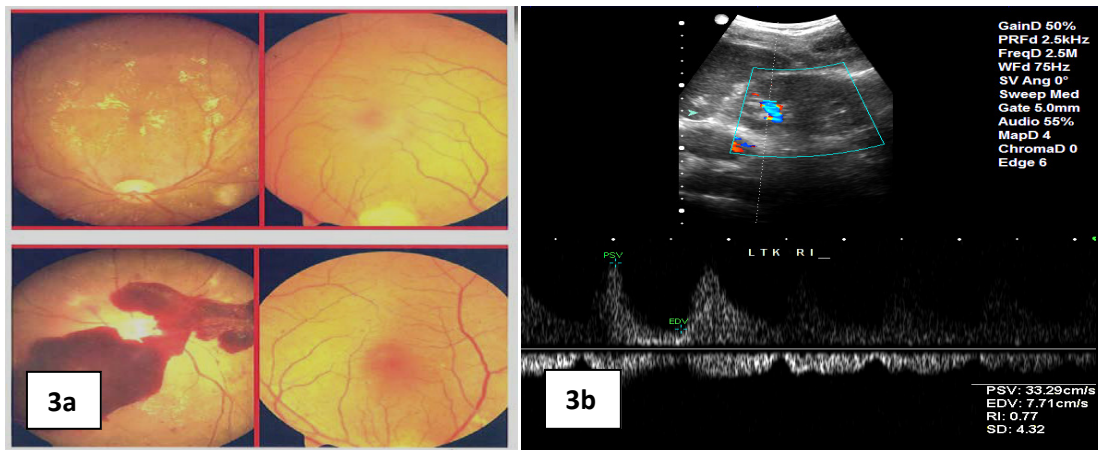


Figure 3: Fundoscopy images (a) – upper two images showing hard exudates involving all four quadrants with dot 'n' blot hemorrhage in more than two quadrants with clinically significant macular edema (severe non proliferative diabetic retinopathy). Lower images showing severe diabetic retinopathy with vitreous hemorrhage. (b) Patient with diabetic retinopathy shows high renal resistive index value (0.77)

Among 35 hypertensive patients, 25 patients are confirmed cases duration ranging from recently diagnosed to greater than 10 years. Remaining 10 cases are suspected cases due to high blood pressure or high total serum cholesterol levels and are waiting

for confirmation. Mean age among females ( $48 \pm 12$ ) is little higher when compared to males ( $41 \pm 15$ ). This data is statistically not significant. The mean duration of hypertension among females is also higher when compared to males. 35 patients are divided into two

groups –group 1 with RI greater than 0.7 (24 in number) and group 2 with RI less than 0.7 (11in number).  $\Delta$  RI variation among the two groups is 0.05 which is statistically significant in our study. Among group 1 patients there is a significant

increase in serum cholesterol and serum creatinine levels ( $\Delta$  serum creatinine 1.72 mg/dl, total serum cholesterol 234 mg/dl) than group 2 patients ( $\Delta$  serum creatinine 0.92 mg/dl, total serum cholesterol 225 mg/dl).

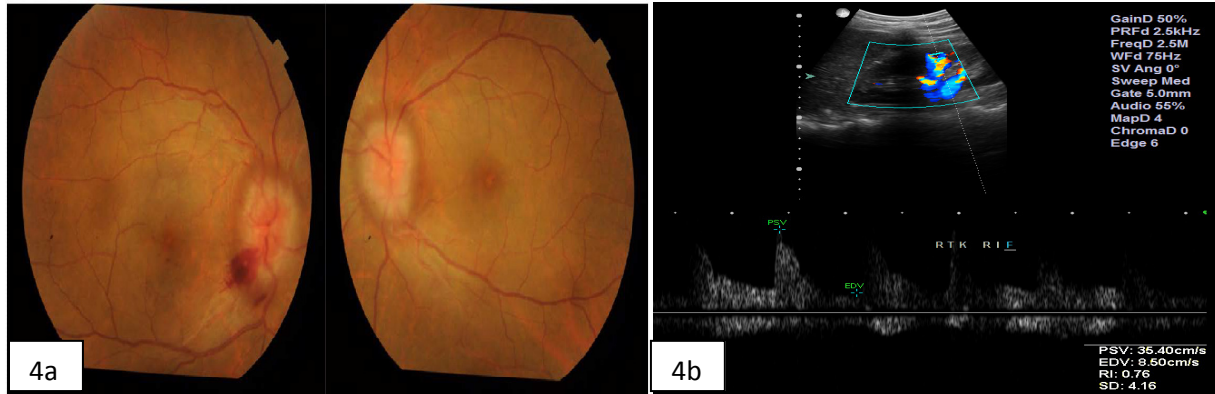


Figure 4: showing funduscopy images(a) with grade 4 hypertensive retinopathy according to keith wagner barker classification. Disc margins are blurred with vessel attenuation. Flame shaped hemorrhages are seen. Macula appears dull. Patient with hypertensive retinopathy shows increased resistive index(0.76) (b).

**Table 1:** showing overall sensitivity, specificity, positive predictive value, negative predictive value and ‘p’ value of the renal resistive index

	Sensitivity	Specificity	PPV	NPV	‘P’ value
Renal obstruction	80	100	100	83.3	<0.0001
Diabetes	84	70	87.50	63.6	<0.0001
Hypertension	88	80	91.6	72.7	<0.0001

**DISCUSSION:**

Renal Doppler Ultrasonography is a highly sensitive and specific test that can be useful in the diagnosis of acute unilateral renal obstruction.<sup>[9]</sup> This is used to measure renal blood flow as well as to calculate RI. The ratio of peak systolic velocity and end-diastolic velocity measured by the Doppler ultrasonography is

defined as RI.<sup>[10]</sup> Previous studies on RI have shown that the threshold RI (measured at the arcuate or interlobular arteries) to identify obstructive uropathy is 0.70, Above which, the dilation can be considered to be of obstructive origin with 93% sensitivity and 100% specificity.<sup>[11,12]</sup> de Toledo et al. reported a sensitivity of 91.8% in patients with complete

obstruction but only 48.1% in those with partial obstruction. In my study, the resistive index value is more for complete obstruction when compared with partial. sensitivity was 87.5% and specificity was 57.7% which is correlating with the other previous studies. renal Doppler US is useful for diagnosing acute renal obstruction within 6–48 hours after the onset of symptoms. de Toledo reported that the RI was significantly higher in patients whose renal colic had lasted at least 24 h. In this study, in all the patients who developed hydronephrosis, the rise in RI occurred before the onset of dilation. According to Shokeir and other authors, there is no significant correlation between the RI and the level of ureteral obstruction, whereas de Toledo showed that proximal obstructions were associated with higher RIs than distal obstructions. In my study resistive index values are elevated in proximally obstructed kidneys when compared with distal obstruction. Duplex Doppler RRI will be useful in patients in whom intravenous contrast agent administration must be avoided (like in pregnancy, contrast related allergy and renal dysfunction) <sup>[13]</sup> According to the results of our study, with 80% sensitivity and 100% specificity, RI is useful for the early identification of renal colic patients in the emergency department, particularly for those who must avoid radiation and contrast agents.

Diabetic nephropathy is a frequent microvascular complication of Diabetes mellitus. In advanced DN, glomeruli become sclerotic, tubuli become atrophic, and interstitial fibrosis is increased. Sclerotic glomeruli may cause increased blood flow resistance measurable at an upstream interlobar artery. Increased interstitial fibrosis may cause elevated RI values. The RI of interlobar arteries seems to be a dependable marker of intrarenal changes. Recently, Ohta *et al.* evaluated the relationship between RI and

pulse wave velocity (PWV, a measure of arterial stiffness), which reflects atherosclerosis, and determined whether renal RI differed depending on the underlying renal disease in 245 patients. They found that the RI of the main renal arteries was significantly higher in patients with DN than in other patients. Boddi *et al.* studied renal RI in patients with chronic tubulointerstitial nephritis. They found that RI measurement allows the early identification of both normotensive and hypertensive patients with chronic TIN, when renal function is still preserved. In a series published more recently Heine *et al.* showed that in patients with chronic kidney disease, intrarenal RI linearly increased with a progressive impairment of renal function and independently reflect both local renal damage and systemic vascular disease. <sup>[14]</sup>

The present study confirms a very good correlation between RI and renal functional parameters with 84% sensitivity and 70% specificity which are correlating with the previous studies.

The evaluation of RRI in hypertensive patients reveals significantly higher values than normotensive subjects, even without overt nephropathy. <sup>[15]</sup> Nevertheless, lower RRI values were associated with low renal and CV target organ damage. <sup>[16]</sup> Parolini *et al.* <sup>[17]</sup> in a group of 86 subjects with hypertensive nephropathies showed that patients with RRI >0.7 were characterized by rapid progression of renal dysfunction and a decrease in eGFR >50% during 6 years of observation. In an observation of 281 patients with CKD, Sugiura *et al.* <sup>[18]</sup> demonstrated the significantly higher incidence of worsening renal function in patients with RRI >0.7. Radermacher *et al.*, <sup>[19]</sup> showed that a very high RRI  $\geq 0.80$  reliably identifies hypertensive patients, who are at risk for the progressive renal disease. Our results suggest that

the RI of intrarenal arteries could be a useful marker for early organ damage and predicts cardiovascular complications in hypertensive patients.

**CONCLUSION:**

Doppler USG is a useful diagnostic tool in unilateral acute renal obstruction and chronic nephropathies. RI values are relatively higher in complete and proximally obstructed kidneys when compared to incomplete and distal obstruction.

Intrarenal RI shows a high level of correlation with serum creatinine and glycosylated hemoglobin levels and can be used as a predictor in patients with advanced clinical diabetic nephropathy. RRI value of  $\geq 0.70$  identifies diabetic and hypertensive patients at risk of progressive renal disease and must be used routinely in patients with the chronic medical renal disease .

In this study we have shown that RRI values are positively correlated with target organ damage in hypertensive patients, indicating that renal vascular resistance is related to hemodynamic and

morphologic alteration of the Cardiovascular system. The evaluation of RRI may predict early CV damage and provide an accurate estimate of overall risk, Which is one of the main elements of most current hypertension management guidelines. The 2003 European guidelines for management of hypertension suggest that high normal BP includes values considered high in high-risk subjects for whom antihypertensive treatment is recommended.

I conclude that Intrarenal resistivity index as assessed by duplex ultrasonography is a non-invasive parameter that can be correlated with the clinical profile and biochemical parameters of renal dysfunction in patients with unilateral acute renal obstruction and chronic medical renal diseases (mainly in type II Diabetes mellitus with diabetic nephropathy and hypertensive nephropathy). It correlates significantly with worsening renal function.

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