

## Original Research Article

# Renal resistivity index is inversely proportional to estimated glomerular filtration rate in chronic kidney disease

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## ABSTRACT

**Background:** Renal resistive index (RRI) measured by Doppler ultrasonography has been associated with severity, rate of progression and mortality in chronic renal failure. Parameters like renal vascular resistance, filtration fraction and effective renal plasma flow have been associated with renal resistivity index in chronic kidney disease patients.

**Methods:** This hospital based cross-sectional study was conducted from April 2016 to August 2017. 100 patients with chronic kidney disease were enrolled. RRI was calculated from the blood flow velocities observed during Doppler examinations of the segmental arteries and estimated glomerular filtration rate (eGFR) was calculated using the chronic kidney disease epidemiology collaboration (CKD-EPI) equation. Spearman Rank-Order Correlation Coefficient was used.

**Results:** A Significant inverse correlation was observed between RRI and eGFR ( $r = -0.347$ ,  $p = 0.0004$ ). It was also observed that older age ( $r = 0.297$ ), higher systolic blood pressure ( $r = 0.365$ ), lower levels of hemoglobin ( $r = -0.34$  for males and  $r = -0.353$  for females) were observed to correlate with higher values of RRI in advanced CKD stages.

**Conclusions:** RRI correlated inversely with eGFR in chronic kidney disease and hence was directly related to the severity of the disease.

**Keywords:** Chronic kidney disease, eGFR, Renal resistivity index

## INTRODUCTION

Chronic kidney disease (CKD) is in the course of becoming a bigger major public health issue. CKD is characterized by a progressive loss of renal function resulting in end-stage renal failure; however, the rate of decline is highly variable. Outcomes of chronic kidney disease include not only kidney failure but also complications of decreased kidney function and cardiovascular disease. So, an early detection and timely management are essential for the medical care of patients with CKD. In clinical practice, information derived from

kidney biopsies is commonly considered a 'gold' standard that establishes the histopathological patterns concerning renal injury. However, biopsies are invasive and may result in various complications, including gross hematuria and may even be contraindicated in various conditions like coagulopathy.<sup>1</sup> Alternatively, Doppler sonography is a non-invasive method of examination that is widely used for the evaluation of patients with CKD which provides valuable data about both the renal morphology and vasculature. The renal intraparenchymal arterial flow pattern is influenced by structural and functional factors, and the flow wave is

created by vascular compliance and resistance. This is why pathological conditions such as interstitial fibrosis have a strong impact on the indices obtained from Doppler examinations.<sup>2</sup>

The renal resistivity index (RRI), measured at the level of the interlobar arteries, is thought to reflect downstream vascular impedance and therefore, has been suggested as a measure of renal arterial stiffness. An increased resistive index has been reported to correlate with glomerulosclerosis (GS), tubulointerstitial damage (TI) and vascular lesions and to predict the rate of progression to end-stage renal disease.<sup>3-5</sup>

This study was conducted to determine the correlation of estimated glomerular filtration rate (eGFR) with RRI in CKD patients and define the relation of RRI with eGFR in CKD.

## METHODS

This observational cross-sectional study was conducted at M L N Medical College and its associated S R N Hospital from April 2016 to August 2017. The study comprised of 100 patients aged  $\geq 18$  years of either sex, with CKD confirmed as per Kidney Disease Outcomes Quality Initiative (KDOQI) guidelines, admitted in the Department of Medicine during this period.

The subjects were properly told about the purpose of the study and a written informed consent in English and Hindi was taken from all the participants in the study. Patients who were a known case of renal artery stenosis, diabetes mellitus, cardiomyopathy, ischemic heart disease and valvular heart disease were excluded from the study.

Demographic data was recorded, and a detailed history was taken from each patient including history of hypertension, diabetes mellitus, and previous episodes of acute kidney injury and symptoms of uremia. Clinical examination including blood pressure measurement, pallor, anasarca, chest crepitations, and pericardial rub were assessed. Baseline investigations were done for enrolled patients. Abdominal Ultrasound was done to look for renal size, echogenecity and corticomedullary differentiation. Serum Urea and Creatinine was measured and simultaneously eGFR was calculated using EPI equation.

$GFR (mL/min/1.73m^2) = 141 \times \min (SCr/\kappa, 1)^\alpha \times \max(SCr/\kappa, 1)^{-1.209} \times 0.993Age$  (Multiply by 1.018 for women) ( $\kappa$  is 0.7 for females and 0.9 for males,  $\alpha$  is -0.329 for females and -0.411 for males).

Doppler ultrasonography of the intrarenal arteries was done; arcuate arteries located on cortico- medullary junction were insonated. Three to Five measurable wave forms from each kidney were obtained and RI was measured from the mean of above values. RI was calculated as follows =Peak Systolic Velocity-End

Diastolic Velocity/Peak Systolic Velocity using the in-built software from the ultrasound unit.

## Statistical analysis

Statistical analysis was done using Statistical Package for Social Sciences (SPSS) version 21.0. Categorical variables were presented in number and percentage (%) and continuous variables were presented as mean  $\pm$  SD. Quantitative variables were compared using Unpaired t-test/Mann- Whitney Test (when the data sets were not normally distributed) between the two groups. Qualitative variables were correlated using Chi-Square test /Fisher's exact test. Pearson correlation coefficient/Spearman rank correlation coefficient was used to assess the association of various quantitative parameters. A p-value of less than 0.05 was considered to be significant.

## RESULTS

A total of 100 CKD patients were enrolled in this cross-sectional study conducted at Swaroop Rani Nehru hospital, Allahabad over duration of 16 months. Table 1 shows the baseline characteristics of the study population.

**Table 1: Baseline characteristics of the study population.**

	Mean $\pm$ Stdev
Age	51.21 $\pm$ 18.26
Gender (Males)	55%
SBP	151.88 $\pm$ 23.4
DBP	95.06 $\pm$ 10.58
MAP	114 $\pm$ 14.28
RBS	105.29 $\pm$ 20.43
S. Urea	79.96 $\pm$ 36.4
S. Creat	3.8 $\pm$ 2.79
eGFR(EPI)	24.93 $\pm$ 15.23
Renal doppler (R.I.)	0.68 $\pm$ 0.08

Upon dividing the study population into four groups based upon age. Maximum number of cases i.e. 38% belonged to 41 - 60 yrs age group with 20 males and 18 females. At the time of admission, the patients were distributed according to CKD stages on the basis of the estimated glomerular filtration rate, as per the KDIGO classification as shown in Figure 1. Majority of the patients were found out to be in the higher stages i.e. 28% patients in stages 4 and 35% patients in stage 5 and none of the patients being in stage 1 or 2.

All the patients were then classified according to their grade of systolic and diastolic hypertension and anemia noticed on general examination and routine investigation. Grading of hypertension was done as described by seventh report of Joint National Committee (JNC-7) and anemia was graded as per the World Health Organization (WHO) guidelines. Majority of patients were in stage 1 and 2 of hypertension (approximately 70%) and most of

the patients were having moderate (55%) to severe (40%) anemia.

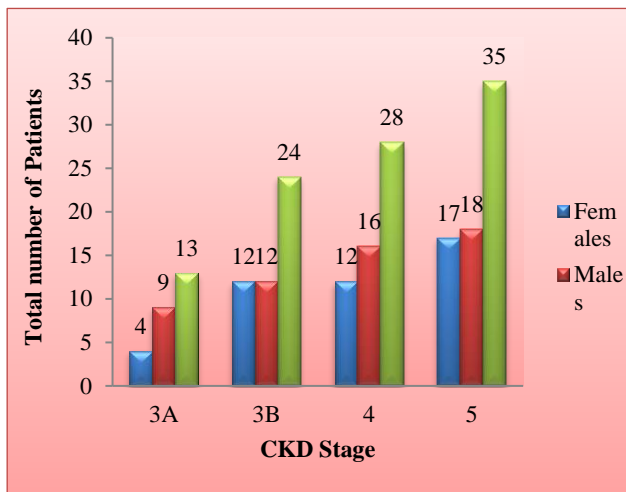


Figure 1: Stage wise distribution of CKD cases.

Figure 2 shows the distribution of cases according to Resistivity index. The patients were divided in to three groups; the cases with values  $\leq 0.65$  were considered to be normal and values greater than 0.70 were considered to be abnormal which was seen in majority (43%) of the cases.

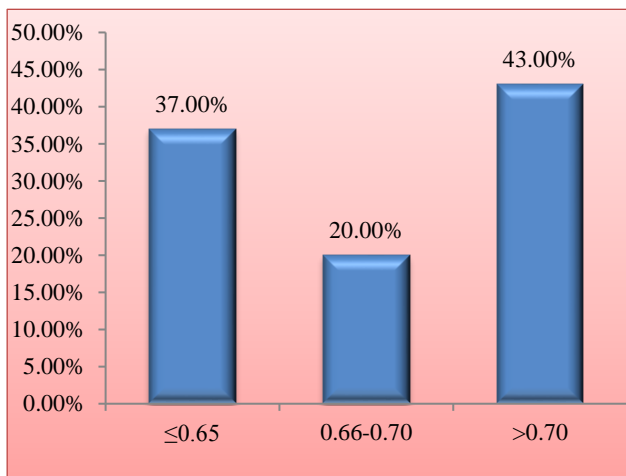


Figure 2: Distribution of cases according to Resistivity index.

Table 2 shows correlation between various factors like blood pressure and hemoglobin levels with eGFR and resistivity index. It was observed that higher systolic blood pressure ( $r = -0.342$ ) and lower levels of hemoglobin ( $r = 0.374$ ) correlated significantly with lower values of estimated glomerular filtration rate and hence advanced CKD stages. Conversely, resistivity index correlated positively with age ( $r = 0.297$ ) and systolic blood pressure ( $r = 0.365$ ); and negatively with hemoglobin levels ( $r = -0.34$ ). However, correlation with diastolic blood pressure was found to be insignificant ( $p = 0.0767$ ).

Table 2: Correlation between various factors, eGFR and RRI.

	eGFR(EPI)		Renal doppler (R.I.)	
	Correlation Coefficient	P value	Correlation Coefficient	P value
AGE	-0.018	0.8585	0.297	0.0027
SBP	-0.342	0.0005	0.365	0.0002
DBP	-0.179	0.0752	0.178	0.0767
Hb (males)	0.374	0.0049	-0.34	0.011
Hb (females)	0.347	0.0194	-0.353	0.0172

A significant correlation was seen between eGFR and Resistivity index with a correlation coefficient of  $-0.347$  which signifies a negative correlation between the two variables thus correlating the higher values of resistivity index with later stages of chronic kidney disease and thus to a poorer prognosis (Figure 3).

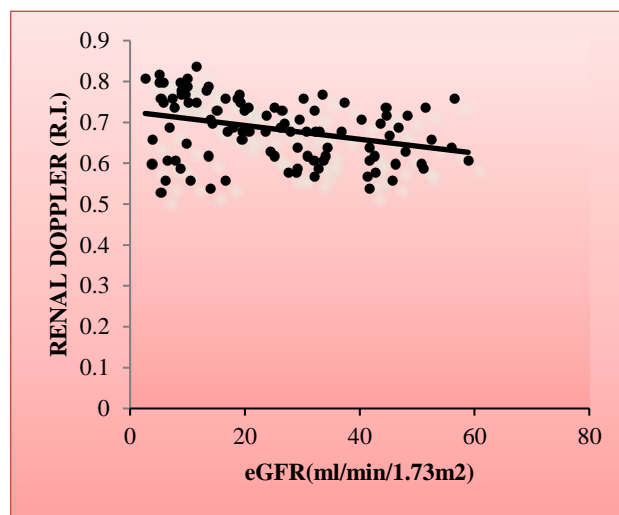


Figure 3: Correlation of eGFR with Resistivity Index.

DISCUSSION

Chronic renal disease is a risk factor for end-stage renal disease and cardiovascular diseases. Early detection and timely management are essential for the medical care of patients with CKD and slow their progression and reduce the associated morbidity and mortality.

Even though previous studies have demonstrated the relevance of Renal Resistivity Index in predicting the progression of renal dysfunction and prognosis in Chronic Kidney Disease patients, their usefulness has not been extensively explored in these patients.

In this cross-sectional study, conducted on 100 CKD cases out of which 55 were males and 45 were females with mean age of  $51.69 \pm 18.54$  years and  $50.62 \pm 18.09$  years respectively. Cases were distributed according to CKD stage at the time of presentation.

Majority of patients (63.00%) were in stages 4 and 5 of CKD i.e. they had an eGFR less than 30 ml/min/1.73 m<sup>2</sup>. However, there were no patients in stage 1 or stage 2 as patients with CKD present after significant loss of renal function. Also, since the study centre is a tertiary care hospital, patients present here late and in more critical stages, which explains the failure to enroll patients in early stages of CKD. Authors found a statistically significant correlation between eGFR and renal resistivity index in patients with chronic kidney disease ( $r=-0.347$ ,  $p=0.0004$ ). Previous studies also confirm that renal resistivity index correlates inversely with eGFR and could be used as a marker of severity and progression of renal disease.

Hanamura et al showed that RI increased with the CKD stage and showed correlations with renal function i.e. eGFR ( $r= -0.52$ ,  $P<0.01$ ) and histological damage scores.<sup>6</sup> They also found that elevated RRI, proteinuria and low eGFR were independent risk factors for CKD progression. Similarly, Sugiura et al found a clear correlation between RI and eGFR ( $r= -0.533$ ).<sup>7</sup> In a study conducted by Bigé et al to analyze the association of RI with identified prognostic factors of CKD and with renal outcome, they observed a significant inverse correlation between RI and baseline eGFR ( $r=-0.402$ ,  $p=0.0018$ ).<sup>8</sup>

Moreover, Parolini et al found a strong correlation between initial RI and final renal function.<sup>9</sup> They showed that the patients with an initial RI of 0.70 or higher showed a rapid decline of renal function independent of initial eGFR. Initial RI not only correlated significantly with eGFR of the initial groups ( $r=-0.38$ ,  $P<0.001$ ) representing its correlation with CKD stage but also with final eGFR on follow-up ( $R=-0.4$ ,  $P<0.001$ ) representing its significance as an independent risk factor for the progression to renal failure.

In present study authors also observed a significant correlation of RI with age ( $r=0.297$ ), Systolic blood pressure ( $r=0.365$ ) and hemoglobin levels ( $r=-0.34$  for males and  $r=-0.353$  for females). With reference to other studies Pontremoli et al showed that RI was positively correlated with age ( $r=0.25$ ) and systolic blood pressure (SBP) ( $r=0.2$ ).<sup>10</sup> Derchi et al found a positive correlation of RI with age ( $r= 0.283$ ) and systolic blood pressure ( $r=0.238$ ).<sup>11</sup> Parolini et al observed a significant correlation among RI, age ( $r=0.28$ ), and systolic blood pressure( $r=0.39$ ).<sup>9</sup> Sugiura et al showed a positive correlation between RI and age ( $r= 0.559$ ) or systolic blood pressure ( $r= 0.36$ ).<sup>7</sup>

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