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Ultrasonographic Evaluation of Renal Resistive Index Among Hypertensive and Normotensive Adults in Nepalese Population

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Abstract

Introduction: The Renal Resistive Index is an ultrasonographic spectral Doppler parameter employed for the assessment of renal hemodynamics. In patients with primary hypertension, it reflects changes in intrarenal perfusion as well as systemic hemodynamics and atherosclerosis. It may provide useful prognostic information and possibly have therapeutic implications. It could be the non-invasive screening tool for early detection of renal damage in primary hypertension.

Aim: The aim of the study was to evaluate Renal Resistive Index among hypertensive and normotensive adults as well as to compare Renal Resistive Index among normotensive/hypertensive groups, different age groups, male /female, severity of hypertension and right /left kidney.

Materials and methods: It was a hospital based prospective observational study. 36 – Hypertensive (case) and 36 – Normotensive (control) were enrolled in the study using convenience sampling technique. Renal resistive index values of the interlobar artery in both kidneys were recorded and compared. Independent t test, Non-parametric test, Mann-Whitney U test and Spearman's rank correlation coefficient were applied for statistical analysis.

Results: In normotensive group, the mean Renal Resistive Index was 0.0594±0.054 on right kidney, whereas 0.594±0.054 on left kidney which was lower than that of hypertensive group with mean of 0.724±0.046 on right kidney and 0.723 ±0.047 on left kidney. This difference was statistically significant on each side of the kidney (p-value-<0.001). There was significant positive correlation between participants age and Renal Resistive Index on right side; r (70)= 0.392 (p< 0.001) and Renal Resistive Index on left side r (70)= 0.379 (p< 0.001). The mean differences among male 0.647±0.085 and female 0.670±0.078 participants were not found to be significant (p=0.239). Similarly, mean Renal Resistive Index was not found to be significant among right and left kidney in both groups.

Conclusions: Renal Resistive Index demonstrates elevated values in individuals suffering from essential hypertension, and it displays a notable correlation with both the severity of hypertension and the patient's age. Its utilization offers a valuable means to assess renal vascular resistance reflecting intrarenal perfusion changes and also indicates systemic atherosclerotic changes. It could be the novel hemodynamic parameter that can aid in screening and monitoring patients with essential HTN as well as assessment of treatment efficacy and early detection of renal damage.

Introduction

Pourcelot, first proposed the Renal Resistive Index (RRI) in 1950 AD for the semi-quantitative measurement of intrarenal vascular resistance[1]. RRI is evaluated using spectral Doppler sonography and is non-invasive and reproducible measure to evaluate renal hemodynamics [2]. Alterations in this parameter have been noted in a range of conditions affecting the kidney, such as acute variations in renal vascular resistance or in systemic hemodynamics[2–4]. RRI is calculated by dividing the difference between the peak systolic velocity (PSV) and end-diastolic blood velocity (EDV) by the PSV in an intrarenal artery (interlobar/arcuate) using Doppler sonography (Fig.1)[5]. The normal range is considered to be 0.50-0.70 [3,6].

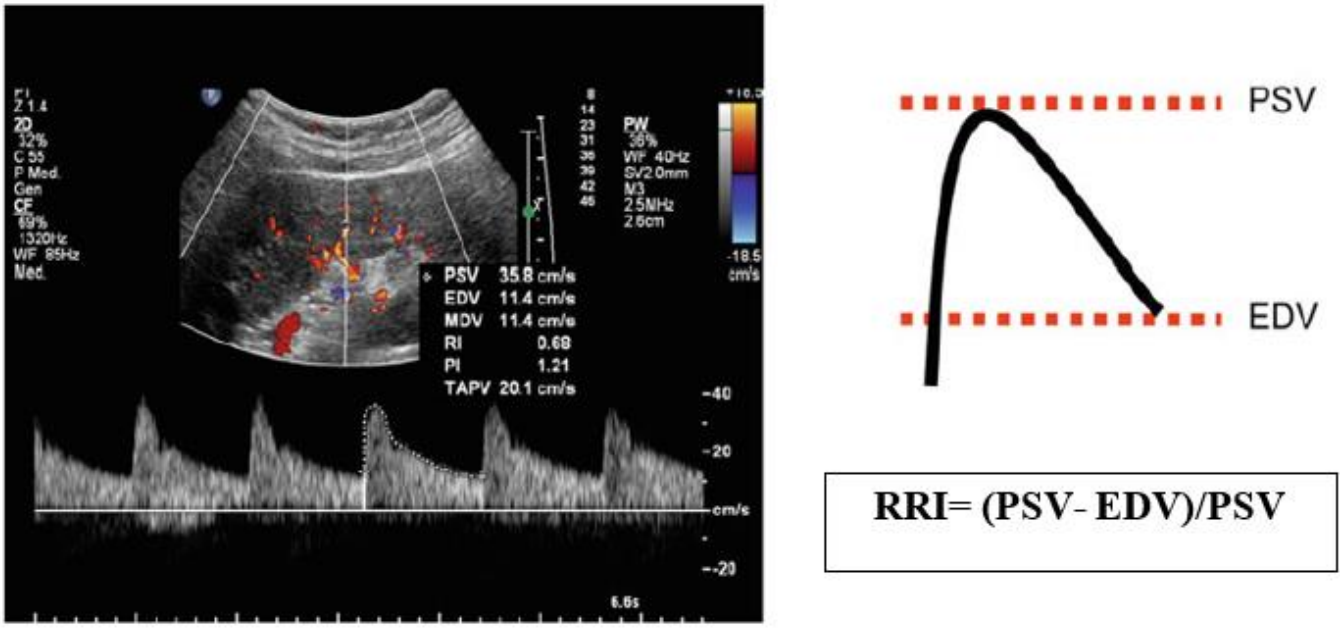

Fig. 1 RRI is measured by Doppler sonography in an intrarenal artery, as the difference between the peak systolic (PS) and end-diastolic (ED) blood velocities divided by the peak systolic velocity (PSV)

Another index called Pulsatibility Index (PI) is also been used to express vascular resistance of renal bed, which is calculated as PI = (PSV - EDV) / Mean Velocity. However, RRI is found to be more reproducible and used commonly in evaluation of renal hemodynamics rather than PI [7,8]

RRI is age-dependent, it is highest at birth, gradually decreases with aging, stabilizes in a specific range 102– 130 months (mean RI range considered normal for adults) and then increases to adult levels[9]. It is dependent on various renal and systemic determinants as shown in Fig.2[10].

Doppler-derived RRI has been used for years in a variety of clinical settings such as the assessment of acute [4,11],chronic renal allograft rejection[12], detection and management of renal artery stenosis [13], urinary obstruction [14], acute tubular necrosis[15], evaluation of progression risk in chronic kidney disease (CKD)[2], differential diagnosis in acute and chronic obstructive renal disease, and more recently as a predictor of renal and overall outcome in the critically ill patient[16,17].

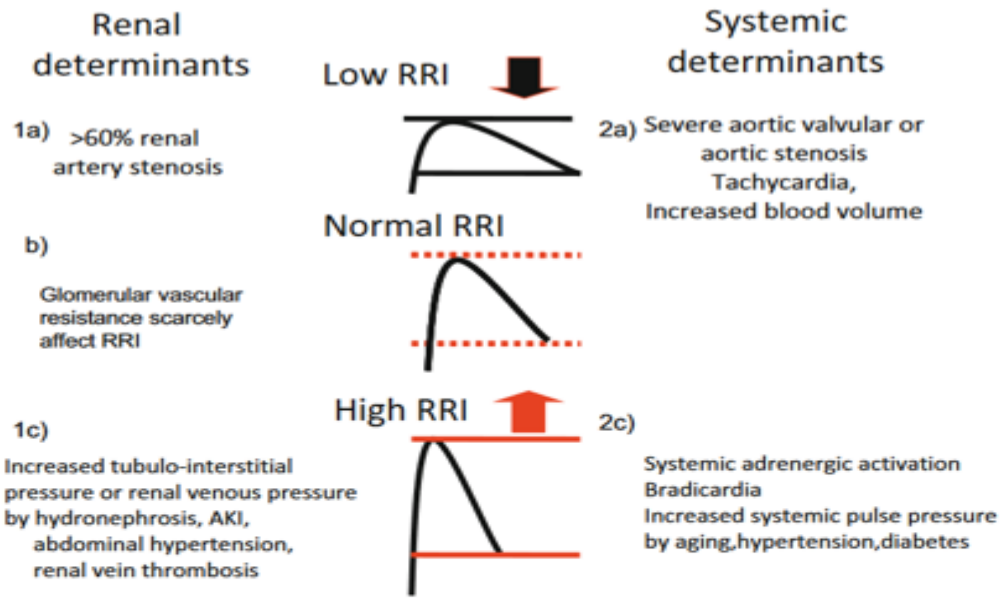

Fig 2: Different renal and extrarenal systemic determinants concur to determine RRI.

(1a) and (2a): renal and systemic determinants that decrease RRI.

(b): glomerular resistance scarcely or not affect RRI.

(1c) and (2c): renal and systemic determinants that increase RRI

(Adapted by Boddi et al. 2015)

1.28 billion adults aged 30-79 years worldwide have hypertension (HTN), with the majority (two-thirds) living in low- and middle-income countries. An estimated 46% of adults with HTN are unaware that they have the condition. Less than half of adults (42%) with HTN are diagnosed and treated.
Approximately 1 in 5 adults (21%) with HTN have it under control. HTN is a major cause of premature death worldwide [(18)]. Over 90% of patients with high blood pressure (BP) have primary HTN [(19)]. The overall prevalence of HTN in Nepal is 24.5% [(20)]. Guidelines for diagnosis and when to commence treatment for HTN, a sustained elevation of systolic blood pressure (SBP) of 140mmHg or diastolic blood pressure (DBP) of 90 mmHg, have been extensively reviewed (Table: 1) [(21)].

Table 1: Classification of Blood Pressure in Adults (Age ≥ 18 years)

Classification	Systolic Blood Pressure (mmHg)		Diastolic Blood Pressure (mmHg)
Normal	<120	AND	<80
Prehypertension	120-139	OR	80-89
Stage I HTN	140-159	OR	90-99
Stage 2 HTN	≥160	OR	≥100

The kidneys are one of the three primary target organs in humans susceptible to injury from HTN. They are located below the diaphragms, unlike the brain or the heart, and as a result, when standing upright, they are exposed to higher ambient pressure loads than the cerebral or coronary arteries [22]. Doppler ultrasonography of the renal vessels has been found useful in the diagnosis of various cause of secondary HTN, renal artery stenosis in the face of equivocal angiogram and in differentiating real renal tumors from pseudo tumors such as a hypertrophied column of Bertin. Increase in renal arterial impedance is an early change in hypertensive nephropathy. It is therefore important to detect this early renovascular change through routine surveillance since intervention at this stage may prevent or at least delay the renal damage [23]. A key diagnostic method for diagnosing essential HTN may also be the assessment of blood flow and anomalies in renal and intrarenal arterioles. In reality, the kidney is invariably affected by hypertensive arteriolar changes in essential HTN, and the renal blood flow may be reduced as a result of arteriolar constriction in the early stages of the condition. The hemodynamic hallmark of established essential HTN is a clearly raised total peripheral vascular resistance [24].

Currently, the majority of clinicians predominantly depend on BP measurements, assessments of proteinuria, and parameters such as glomerular filtration rate (GFR) or creatinine clearance when evaluating hypertensive patients and forecasting the future course of chronic kidney disease. This preference likely arises from the fact that standard grey scale ultrasound studies primarily focus on aspects such as renal length, volume, echogenicity, cortical thickness, and the pelvicalyceal system. While renal echogenicity and size do exhibit a strong correlation with histopathological findings, their utility primarily lies in evaluating the chronicity of the disease. In the early stage of the disease, there may be no significant change in the gross appearance of the kidneys.[25] In clinical practice albuminuria is measured to define subclinical renal damage in hypertensive patients, and the combination of Estimated Glomerular Filtration Rate (eGFR) and albuminuria is a useful predictor of Cardiovascular disease(CVD).[25] The relationship between RRI and renal function in primary HTN was subsequently investigated in greater detail in a larger cohort of patients, and it was shown that increased impedance to blood flow at the parenchymal level is often associated with a mild reduction in GFR, increased albuminuria or both[26]. In recent years RRI is also validated as a clinical marker of subclinical renal damage as well as a prognostic predictor of renal and CV outcomes to use in addition to the above mentioned markers in order to improve their performance [27].

Recent clinical and experimental evidence indicates that an increased RRI in patients with primary HTN not only reflects changes in intrarenal perfusion, but that it is also associated with systemic hemodynamics and atherosclerosis, and may provide useful prognostic information and possibly have therapeutic implications[28,29,34] . It has been shown that Angiotensin-converting enzyme inhibitors / Angiotensin II Receptor Blockers (ACE/ARBs) treatment was associated with significant decrease of RRI compared to other drugs [beta blocker (BB) and calcium channel blocker (CCB)], indicating their more renal protective effect[34].

The purpose of this study was to evaluate RRI in patients with essential (primary) HTN and in normal controls. Correlation of RRI with age, sex and severity of HTN was also analyzed along with evaluation of RRI difference among right and left kidney.

Material and methods

Prospective observational study was conducted in Department of Radiodiagnosis and Imaging, National Academy of Medical Sciences (NAMS), Bir Hospital, Kathmandu, Nepal from July 20, 2023 to October 17, 2023 . Following ethical clearance from Institutional Review Board (IRB), 36 cases were enrolled in hypertensive (case) and 36 cases in normotensive (control) group.

Inclusion criteria

For hypertensive:

Participants age ≥35 years and any one of following criteria:

- Patient already diagnosed as systemic HTN not under medication.
- SBP ≥140 and /or DBP ≥ 90.

For control arm:

- Healthy normotensive individuals

(Those with SBP ≤140 mmHg and DBP ≤90 mmHg) matched for age coming to the radiology department for other investigations.)

Exclusion criteria

For Hypertensive /control arm

- Those aged <35 years
  (Essential HTN most often occurs first during the middle-age years which begins at 35 years and ends around 68 years) [23].
- Secondary hypertension (renovascular or endocrinal)
- Clinical or sonographic signs of any renal disease (eGFR < 60 ml/min/1.73m2 or serum creatinine above 2.0 mg/dl)
- Pregnancy
- Cardiovascular disease (as congenital, rheumatic, ischemic heart diseases or heart failure)
- Other marked systemic diseases (as malignancy, diabetes, cirrhosis of the liver, obstructive pulmonary disease, severe obesity, sickle cell disease)
- Ascites

Ultrasound machine- SIUI Apogee 5300 with curvilinear 2-6MHz Transducer was used. The participant laid down supine on the examining couch. The skin of the lumbar region was covered with ultrasound gel, and the probe was applied to it. The appropriate depth of focus, frame rate and gain setting was adjusted to obtain an optimal image. B-Mode, colour Doppler and spectral Doppler ultrasound were used in the study. The abdominal aorta and the main renal arteries were first checked to identify possible plaques and stenosis in B-mode. Global examinations of the kidneys were performed. Using color and spectral Doppler, sampling for RRI was done at the level of the interlobar arteries (adjacent to medullary pyramids. Then, the measurements were repeated in different parts of both kidneys (superior, median, and lower) when at least three reproducible waveforms had been obtained. Then, RRI was calculated with the following formula: (peak systolic velocity – end diastolic velocity)/peak systolic velocity and the mean value of three measurements at each kidney were considered.

For Optimization of Doppler study following parameters was adjusted:

- Optimal insonation angle <30 degree.
- Lowest pulse repetition frequency without aliasing.
- The highest possible gain without noise.
- The lowest wall filter /gate of 2–4mm (adjusted as necessary).

The data were entered in electronic database (MS Excel 2010) and was analyzed by transferring it to Statistical Package for the social sciences (SPSS) version 24. Data was analyzed using appropriate statistical methods. Independent t test was applied to compare the continuous variables between two groups. Non parametric test, Mann-Whitney U test was applied to compare two continuous variables but not normally distributed. The linear correlation between variables was evaluated by the nonparametric rank correlation Spearman test. The significance level was set at 5% (p-value < 0.05). The results were expressed in tables, bar diagram and pie chart. Descriptive statistical tools like frequency, percentage, median, interquartile range (IQR) mean, and standard deviation were used to express the result.

Results

36 participants were enrolled in each groups. 44.4% cases were male in hypertensive group and 55.6 % cases were male in control group. The minimum and maximum age of the participants were 30 years and 98 years respectively with mean age 50.03 (±15.13) years. The mean rank of participants in hypertensive and normotensive groups were 42.49 and 30.51 respectively. It was found that there was age difference in two study groups and was statistically significant (p value: 0.016) (Table 2)

Table 2: Comparison of age of the participants in study groups

Variables	Hypertensive Mean rank	Normotensive Mean rank	p-value
Age	42.49	30.58	0.016

P-value is significant at <0.05

In normotensive group, the mean RRI was 0.594±0.054 on right kidney whereas 0.594±0.054 on left kidney which was lower than that of hypertensive group with mean RRI 0.724±0.046 on right kidney and 0.723±0.047 on left kidney. This difference was statistically significant on each side (p-value-<0.001) (Table 3). The result also showed that the mean intrarenal artery resistive index (RI) was same on right and left kidney in both study group.

Table 3: Comparison of RRI in hypertensive and normotensive

Renal parameters	Hypertensive Mean±SD	Normotensive Mean±SD	t- value	95%Cl	P-value
Right intrarenal (interlobar) artery RI	0.724±0.046	0.594±0.054	10.92	0.106-0.154	<0.001
Left intrarenal (interlobar) artery RI	0.723±0.047	0.594±0.054	10.69	0.104-0.152	<0.001

P-value is significant at <0.05

The mean right RRIs was 0.692±0.039 among stage I hypertensive participants and the mean RRI among participants with stage II HTN was 0.733±0.004. This showed that RRI is more in stage II HTN participants compared to stage I HTN. The difference was found to be statistically significant (p=0.018) (Table 4).

Table 4: Intrarenal resistive Index in Hypertensive (stage I and II) participants

Renal parameters	Stage I Mean±SD	Stage II Mean±SD	P-value
Right intrarenal (interlobar) artery RI	0.692±0.039	0.733±0.004	0.018
Left intrarenal (interlobar) artery RI	0.692±0.033	0.731±0.047	0.025

P-value is significant at <0.05

The study showed that among all participants the mean RRI difference among male and female participants were not found to be significant . Likewise, mean left intrarenal (interlobar) artery RI was not significantly different according to sex (male: 0.645±0.089; female: 0.672±0.072; p-value -0.161) (Table 3).

There was significant positive correlation between participants age and RRI on right side; r(70)= 0.392 (p< 0.001) and RRI on left side r(70)= 0.379 (p< 0.001) (Table 5). This showed that RRI increases as the age advances.

Table 5: Correlation of Age with RRI

Correlations

			AGE	RIGHT RRI	LEFT RRI
Spearman's rho	AGE	Correlation Coefficient	1.000	.392**	.379**
		Sig. (2-tailed)	.	<.001	.001
		N	72	72	72
	RIGHT RRI	Correlation Coefficient	.392**	1.000	.965**
		Sig. (2-tailed)	<.001	.	<.001
		N	72	72	72
	LEFT RRI	Correlation Coefficient	.379**	.965**	1.000
		Sig. (2-tailed)	.001	<.001	.
		N	72	72	72

**. Correlation is significant at the 0.01 level (2-tailed).

Discussion

RRI is spectral Doppler parameter used to evaluate renal hemodynamics. It is non-invasive and reproducible parameter which shows alterations in range of conditions affecting kidney and systemic hemodynamics [1,2] . The overall prevalence of HTN is increasing worldwide. The kidneys are one of the three primary target organs in humans susceptible to injury from HTN. A key diagnostic method for diagnosing essential HTN may also be the assessment of blood flow and anomalies in renal and intrarenal arterioles. Since RRI correlates well with the early marker of renal damage by HTN like albuminuria and eGFR. RRI could be the non invasive screening tool for early detection of renal damage in primary HTN. The objective of this study was to evaluate RRI among hypertensive and normotensive adults in Nepalese populations. This study showed that, in normotensive group, mean ± SD, RRI was 0.0594±0.054 on right kidney and 0.0594±0.054 on left kidney. These findings were comparable to, that of Madubueze et al [23], who reported mean interlobar artery RI values of 0.59 ± 0.04 and 0.59 ± 0.03 on the right and left sides, respectively, in normotensive control individuals. Although slightly higher than, that of Atalabi et al. [35] in south-western Nigeria, who reported 0.56 ± 0.04 (range = 0.48–0.67) and 0.56 ± 0.04 (range = 0.48–0.65) on the right and left sides, respectively. Viazzi et al.[37] in the United States showed that the average RRI of 15 native kidneys from eight patients with no known renal abnormalities was 0.60, which is highly comparable with the findings of this study. Galesic et al [24] in Croatia studied 67 normotensive controls showed RRI of 0.596 ± 0.038, which is comparable to this study. Elshimy et al [38] also showed RRI (0.60 ± 0.02) in normotensive control group, which is comparable to this study.

The findings of this study of the mean RRI in the hypertensive group being 0.724±0.046 and 0.723±0.047 on right and left side were in concordance with that of Madubueze et al[23], who reported mean RRI values of 0.73 ± 0.03 on both sides , in hypertensive individuals. Similar comparable results were also obtained by Elshimy et al[38],which showed RRI of (0.71 ± 0.04) in hypertensive group. These findings were comparable to that of , Platt et al.[39] who reported that a mean RRI value < 0.70 can be used as an indicator of normal renal vascular resistance in adults; while a mean RRI value > 0.70 can be interpreted as a sign of elevated renal vascular resistance, which can be found in several renal parenchymal diseases such as essential HTN. However, Mastorakou et al.[30] reported that higher values of RRI > 0.70 can also be seen in elderly subjects (seventh decade and above) without renal dysfunction. This could be due to the fact that with aging there is a tendency of vascular compromise that may occur from atherosclerosis that may be responsible for elevation of renal RI [40]. Although, the main renal arteries and the abdominal aorta were examined first in this study for potential plaques and stenosis but the normal results do not rule out the possibility of early atherosclerotic alterations in the small intraparenchymal renal vessels. However, Atalabi et al [34] showed that mean RRI in the hypertensive group (n= 72) was 0.60 ± 0.04 , which was lower as compared to this study.

This study showed no significant difference in mean RRI among right and left side in both groups (normotensive and hypertensive). These findings are in concordance with studies conducted by Mastorakou et al.[30] in the UK , Murat et al.[41] in Turkey, Madubueze et al.[23] and Atalabi et al.[34] in Nigeria.

The relatively higher mean renal RIs in the hypertensive group (0.72 on each side) when compared with the normotensives (0.59 on each side); P-value <0.001, is in concordance with the findings of Madubueze et al.[23] , who reported mean RRI of 0.73 and 0.59 in hypertensive and normotensive groups respectively. These findings are in concordance with Elshimy et al [38]. Galesic et al.[24] reported that the mean renal RI in hypertensive patients was 0.66 ± 0.05, which is higher than that in healthy normotensive individuals

(mean RI 0.60 ± 0.03); however, this study, conducted by Galesic et al. in Europe (0.66 ± 0.05), reported a RI that was significantly lower than that of the African counterpart, which may be attributed to genetic and environmental variations. Similar relatively lower RRI in hypertensive patients was noted in study conducted by Ozelsancak et al.[33] in their evaluation of 61 hypertensive patients and 40 healthy controls (0.60 ± 0.04 versus 0.56 ± 0.04) in Turkey. According to According to Pontremoli et al.[(42)], "this increase in mean renal RI value is an early sign seen in adults with essential HTN as a result of HTN-induced myointimal hyperplasia of the renal arterioles. RRI may also be considered as a marker of systemic vascular changes and therefore a predictor of increased cardiovascular risk [(43,44)].

This study showed that the mean±SD left intrarenal (interlobar) artery RIs was 0.692±0.033 among stage I hypertensive participants and the mean±SD left intrarenal (interlobar) artery RIs among participants with stage II HTN was 0.731±0.047. This showed that intrarenal artery resistance index is more in stage II HTN participants compared to stage I HTN. The difference was found to be statistically significant (p=0.025). These findings are in concordance with Galesic et al[.(24)] which showed RRI of 0.64±0.033 and 0.667 ±0.017 in stage I and stage II HTN. Multiple studies showed positive correlation of RRI with SBP or DBP but few study available that studied correlation of RRI with stage of HTN.

The findings of this study mean RRI among male and female participants were 0.647±0.085 and 0.670±0.078 respectively, which was found to be statistically not significant (p=0.239). These results were in concordance with Sigrici et al [(31)] , Atalabi et al.[(34)] In this study among normotensive participants the mean right intrarenal (interlobar) artery RI among male and female participants were 0.583±0.045 and 0.607±0.063 respectively. The mean differences were not found to be significant in overall participants and in hypertensive group. However, left intrarenal (interlobar) artery RI was significantly different according to sex in normotensive group (male: 0.578±0.043; female: 0.615±0.061; p-value -0.044).. Study by Ponte et al.[(6)] showed that RRI was positively associated with female sex in hypertensive than in normotensive participants (0.66±0.06 versus 0.62±0.05; *P*<0.001). This could be due to small sample size or may be due to effect of other determinants of RRI and needs further evaluation.

In this study, mean rank of participants age in hypertensive and normotensive groups were 42.49 and 30.51 respectively which was statistically significant (p value – 0.015). There was significant positive correlation between participants age and RRI on right side; r (70)= 0.392 (p< 0.001) and RRI on left side r (70)= 0 .379 (p< 0.001). These findings are in concordance with Galesic et al. (r = +0.62, p < 0.0001)[24] and Ponte et al.[(6)] who showed that RRI positively correlated with age in women and men (both R=0.41; P<0.001), although the relationship was not linear (age^2, R=0.14 and R=0.16; both P<0.005). This findings suggests increase in stiffness of systemic as well as renal vascular resistance with advancing age. However Sigrici et al[(31)] showed RRI tended to decrease with increasing age (r= -0.732). Atalabi et al.[(35)] showed no correlation between RRI and age.

Conclusions

This study showed that, RRI is increased in patients with essential HTN and it correlates with degree of hypertension and age. Utilization of the RRI enables us to evaluate renal vascular resistance, which provides a new hemodynamic parameter in the screening, follow-up of patients with essential hypertension and in the evaluation of antihypertensive drug therapy by monitoring the influence of drugs on RRI. RRI could also be the non-invasive screening tool to detect early renal damage and with early detection and intervention, irreversible renal damage may be prevented.

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