Original Article

Relation between renal resistive index in children with nephrotic syndrome

Hage Niku[1], Pranoy Dey[2]

From [1]Postgraduate Trainee, Department of Pediatrics, Assam Medical College and Hospital, Dibrugarh, Assam, India, [2]Professor, Department of Pediatrics, Assam Medical College and Hospital, Dibrugarh, Assam, India

ABSTRACT

Context: Renal resistive index (RRI) is a non-invasive marker of several kidney diseases. It is an indicator of resistance to flow within the kidneys, which is a calculation of relationship between systolic and diastolic renal pressure changes. However, there is a limited knowledge in the use of RRI in the management and prognostication of Nephrotic syndrome. **Aims:** The aim of this study was to see the relation of RRI with Nephrotic syndrome. **Materials and Methods:** This hospital-based analytical study was conducted over a period of 1 year (June 2019–May 2020) in a tertiary care teaching institution. All the Nephrotic syndrome cases admitted in the pediatric ward were included in the study after taking consent from the parents/guardians. USG renal Doppler was done and blood and urine investigations were done. The RRI recorded from renal Doppler was compared with different categories of Nephrotic syndrome. **Results:** A total 63 children admitted with Nephrotic syndrome were included in the study. The mean RRI value was 0.66±0.14, 0.64±0.15 and 0.66±0.12 as well as 0.63±0.12, 0.67±0.16 and 0.71±0.13 on the right and left kidney, respectively, for each upper, middle, and lower pole interlobar renal arteries. Thus, the average RRI value of right kidney was 0.65±0.09 and left kidney was 0.67±0.09. Neither of the kidneys showed significant relationship between RRI of different poles. **Conclusion:** In our study, we could not find the USG Doppler useful to predict the disease outcome in children with Nephrotic syndrome.

Key words: Nephrotic syndrome, Renal resistive index, Serum albumin, Serum creatinine, USG renal Doppler

Renal resistive index (RRI) is a calculation of the relationship between systolic and diastolic renal arterial pressure. It is an indicator of the resistance to flow within the kidney. Vascular changes can be assessed by doing non-invasive color Doppler. RRI has been shown as a prognostic instrument in assessing the progression of kidney disease; especially, in hypertension and proteinuria [1]. Normal RI is approximately 0.6 (range: 0.56–0.66). The generally acceptable normal value of the RRI is taken as ≤0.7 [2]. However, a slightly higher RI value (0.72±0.03) has been shown in healthy young children of age four and a half years and below. An initially high RI denotes poor prognosis. This eventually leads to more disease progression.

Studies have demonstrated that high RI, proteinuria, and hypertension are known risk factors for the progression of chronic kidney disease [3]. RI increases in various kidney diseases [4-12], and previous studies have shown the associations of RI with the kidney function and prognosis [13-17]. However, there are not many studies to show the significance of RRI in Nephrotic syndrome (NS) as a prognostic indicator or as an indicator of disease progression. Therefore, this study was planned to evaluate the significance of RRI as a non-invasive marker of severity of NS and to study the relation of increased RI with different blood and urine parameters, that is, serum albumin, serum creatinine, and proteinuria.

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MATERIALS AND METHODS

This hospital-based analytical study was conducted in a tertiary care teaching institution of East India over a period of 1 year (June 2019–May 2020). Prior approval was obtained from the Institutional Ethics Committee and consent was taken from the parents/guardians of all the subjects. All children <12 years of age admitted with NS in the pediatric ward were included in the study. Diagnosis of NS was made on the basis of following criteria: proteinuria >40 mg/m²/h, urine protein:creatinine ratio ≥2, hypoalbuminemia ≤2.5 g/dl and edema. Children >12 years and the guardians who did not give consent were not included in the study.

Data regarding age, gender, locality, socioeconomic status, and clinical features were recorded in a predesigned pro forma. The relation between RRI and NS, along with several blood and urine parameters (serum albumin, serum creatinine and

Correspondence to: Dr. Pranoy Dey, Department of Pediatrics, Assam Medical College and Hospital, Dibrugarh, Assam, India. E-mail: nikuhage37@gmail.com

proteinuria), was seen. Normal value of the renal RI was taken as ≤0.7 [2]. Detailed history, clinical examination, and relevant laboratory and radiological investigations, including color Doppler ultrasonographic study of the renal arteries, were done. Blood sample was sent for serum albumin and renal function test. Bowel preparation was done for 2 days before USG Doppler by advising the patient to take tab festal 1 tab once at bedtime and tab dulcolex 1 tab twice daily.

USG Doppler study was performed by an experienced radiologist using 2.5- to 5-MHz curved array transducers for adequate depth of penetration to visualize the abdominal aorta and its major branches. Proper color Doppler adjustment was done to "screen" the vessel quickly for stenosis because elevated velocities in stenotic regions then produce a color aliasing artifact that is readily apparent. Our sonographer preferred the decubitus or oblique positions because they can use the liver and kidneys as acoustic windows to visualize the renal arteries. The spectral Doppler examination was performed with a small sample volume so as to obtain flow information from only the vessel of interest. Angles of greater than 60 degrees were never used.

Flow abnormalities at the origin of the celiac and superior mesenteric arteries were looked for that indicates significant stenosis. Echogenicity and thickness of the renal parenchyma was noted and the kidney length measured. A longitudinal survey of the abdominal aorta was performed. This was done with both gray-scale and color flow Doppler. Gray-scale evaluation was important to assess for irregular plaque and ostial lesions (i.e., at the origin of the aortic branches), which may be obscured by color flow blooming. Finally, angle-corrected PSV measurements were obtained from the abdominal aorta at the level of the renal arteries. These aortic velocity measurements were used to determine the renal artery–aorta velocity ratio. We had begun at the celiac axis or the superior mesenteric artery because these are easily located, and moved slightly caudal along the aorta until the origin of each renal artery was seen.

The left renal artery was better seen by positioning the patient in a right lateral decubitus position and scanning from a left posterolateral transducer approach, using the left kidney as an acoustic window. Each renal artery was examined with color flow imaging from its origin to the hilum of the kidney, including the main hilar branches. We looked for areas of high-velocity flow, indicated by color shifts or aliasing, as well as turbulence-related flow disturbances, as these may be related to stenosis. Finally, waveforms were also obtained from the segmental arteries in the upper, mid, and lower poles of each kidney. Thus, at least, seven waveforms were captured from each side. This was accomplished by adjusting the spectral display so that the waveforms were large and easily measured.

RI was determined by assessing systolic and diastolic blood velocity in the segmental arteries and applying the following formula: peak systolic velocity-end diastolic velocity/peak systolic velocity. The serum albumin and creatinine were derived by analyzing the subject's serum, and they were compared to the locally standardized laboratory values. The urinalysis is, however, derived using the qualitative method of dipstick using the standardized color.

The statistical analysis of data was performed using the computer program, Statistical Package for the Social Sciences (SPSS for windows, version 21.01, Chicago, SPSS Inc.) and Microsoft Excel 2010. Results on measurement are presented as mean±standard deviation and are compared using Analysis of Variance (ANOVA). Where the p-value was found significant ($p < 0.05$) among three groups, *post hoc* analysis was done to find out the significance between two individual groups. Discrete data are expressed as number (%) and are analyzed using Chi-square and Fischer's exact test. Pearson's and correlation coefficient® was used to measure the associations among continuous variables. For all analysis, the statistical significance was fixed at 5% level ($p < 0.05$).

RESULTS

In our study, total 63 children with NS were included; out of these, 15 (23.81%) were in preschool age ≤5 years and 48 (76.19%) were school going (>5 years). The mean age of the children was 6.39±2.62 years with male:female ratio of 1.52:1. The age of diagnosis of NS among the cases ranged between 2 years and 6 years (mean = 4.68±2.26 years.)

The mean albumin level in the cases of our study was 1.82±0.32 gm/dl. The majority (60.32%) showed 4+ proteinuria in urinary examination. Thirty-four cases were ≤ 6 years, of which 22 cases (34.92%) showed serum creatinine value > 0.5 mg/dl and the rest 12 cases (19.05%) showed the value between 0.2 and 0.5 mg/dl. Twenty-nine children were > 6 years old; out of which, seven cases (11.11%) presented with serum creatinine value of > 0.8 mg/dl, and the rest 22 cases (34.92%) showed value between 0.4 and 0.8 mg/dl. Mean serum creatinine value was 0.56±0.23 mg/dl.

The mean RI value was 0.66±0.14, 0.64±0.15, and 0.66±0.12 as well as 0.63±0.12, 0.67±0.16, and 0.71±0.13 on the right and left kidney, respectively, for each upper, middle, and lower pole interlobar renal arteries in NS cases. The average RI value of right kidney was 0.65±0.09 and left kidney was 0.67±0.09 (Fig. 1). Table 1 shows the correlation of RRI in each pole with different categories of NS. Neither of the kidneys showed significant relation between RRI and different category of NS.

DISCUSSION

Nephrotic syndrome as a cause of renal parenchymal disease gives various sonographic patterns which include changes in parenchymal echogenicity, corticomedullary differentiation, and kidney size. In addition, RRI has been shown to be of high prognostic value in chronic kidney disease; especially, in proteinuric states to which NS belongs. The mean age of children in our study was 6.39±2.62 years, which is higher than the average found in Safaei *et al*. [18] and Bakkali *et al*. [19]. The mean age at the time of diagnosis of NS was 4.68±2.26 year (range 2–6 year) with male:female ratio of 1.52:1 showing male preponderance as seen in other studies [20,21]. The mean serum albumin was 1.82±0.32 gm/dl which was also seen in Hossain *et al*. [22].

Table 1: RRI in different categories of Nephrotic syndrome

Category	Right kidney			p value	Left kidney			p value
	n	Mean	SD		N	Mean	SD	
Upper pole								
1st Episode	18	0.66	0.12	0.9756	18	0.61	0.10	0.0867
Frequent relapse	12	0.67	0.14		12	0.70	0.21	
Infrequent relapse	33	0.66	0.15		33	0.62	0.07	
Middle pole								
1st Episode	18	0.65	0.12	0.8354	18	0.70	0.14	0.5124
Frequent relapse	12	0.62	0.23		12	0.70	0.16	
Infrequent relapse	33	0.65	0.14		33	0.65	0.17	
Lower pole								
1st Episode	18	0.64	0.11	0.7176	18	0.69	0.13	0.6602
Frequent relapse	12	0.66	0.10		12	0.73	0.11	
Infrequent relapse	33	0.67	0.14		33	0.72	0.14	

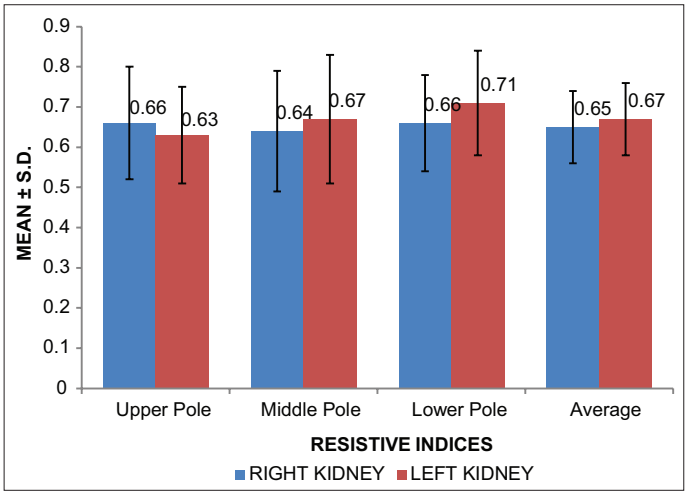

Figure 1: Correlation between mean RRI and NS in different poles of both kidneys

Seven cases (all >6 years) showed the serum creatinine value > 0.8 mg/dl, where the RI was between 0.65±0.18 to 0.74±0.29 in the right kidney and between 0.66±0.10 and 0.84±0.10 in the left kidney (p = 0.0481). Study by Platt *et al*. [13] found a weak correlation between creatinine level and RI value with mean creatinine level of 3.7±3.6.

The relationship between RRI and different categories of NS in both the kidneys showed that there was no significant correlation between the aforementioned parameters (p = 0.9756 and 0.0867 in upper pole of the right and left kidney, respectively, p = 0.8354 and 0.5124 in middle pole of the right and left kidney, respectively, and 0.7176 and 0.6602 in lower pole of the right and left kidney, respectively. In a study Omolola *et al*. [23], comparison of RRI in NS was made between the cases and controls, which showed the only significant mean in the left middle pole (mean RI of 0.58 in cases), irrespective of the category.

In the study Platt *et al*. [5], it has been shown that kidney disease essentially limited to the glomeruli with no active abnormalities in the tubulointerstitial region and no vasculitis, the mean RI was 0.58±0.05. In fact, despite many kidneys having severe or acute glomerular disease, no kidney with disease essentially limited to the glomeruli had an abnormal Doppler waveform. Hence, no further comparison could be made.

There were a few limitations of our study. As the study was conducted for a short duration, long-term follow–up, especially for the relapse cases, could not be done. Moreover, as there was no control group, significant comparison could not be made. Many confounding factors, such as a family history of hypertension, diabetes, chronic kidney diseases, malnutrition, and obesity, were also not taken into consideration. More studies and stronger evidence are needed to see whether RI can be considered as a prognostic indicator in Nephrotic syndrome.

CONCLUSION

In our study, we could not find a significant correlation between RRI and the severity of Nephrotic syndrome. Due to lack of evidence and limited studies, USG renal Doppler cannot be used for prognostication of the disease severity in cases with Nephrotic syndrome and also to predict the disease outcome.

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