THE RENAL ARTERIAL RESISTIVE INDEX AND STAGE OF CHRONIC KIDNEY DISEASE IN PEDIATRIC PATIENTS WITH CHRONIC KIDNEY DISEASE

Fatina Fadel[1], Rasha Essam Eldin [2], Sally Emad -Eldin [3], Shaimaa Sayed[4], Reham Osama[5], Hend Mohamed[6]

Article History: Received: 20.06.2023 **Revised:** 25.07.2023 **Accepted:** 01.08.2023

Abstract

Background: Chronic kidney disease (CKD) is an important health problem. Renal fibrosis serves as an important biomarker in the diagnosis of renal diseases. Its gross anatomy mainly shows that the tissue becomes hard.

Objective: to determine the correlation between resistive index measurements with glomerular filtration rate reduction among children with chronic kidney disease.

Methods: The study is across-sectional study that enrolled 58 children with CKD stage 3, 4, 5. Renal Doppler was performed to measure the resistive index of renal arteries. Then, Correlation between Resistive index and CKD stages were performed.

Results: The right kidney RI was significantly increased gradually with CKD stages. It was significantly higher among Stage 5 (0.65±0.10) than Stage 3 (0.54±0.15) and Stage 4 (0.58±0.11), (p=0.044). In this concern, the left kidney resistive index was increased in stage 5 compared to stages 3 and 4, but the difference between them did not reach a significant level (p = 0.227).

Conclusion: With increase of CKD stage, the degree of renal parenchymal resistance gradually progresses, and the resistive index values increase.

Keywords: Children chronic kidney disease Doppler ultrasound Resistive Index

1 Professor of Pediatrics, Faculty of Medicine Cairo University, Egypt
2 Professor of Pediatrics , Faculty of Medicine Cairo University, Egypt
3 Professor of Diagnostic and Interventional Radiology, Faculty of Medicine, Cairo University, Egypt
4 Lecturer of Pediatrics, Faculty of Medicine Cairo University, Egypt
5 Lecturer of Diagnostic and Interventional Radiology, Faculty of Medicine Cairo University, Egypt
6 M.Sc. Pediatrics, Faculty of Medicine Cairo University, Egypt
* **Corresponding author**: Hend Mohamed **Email:** hendmohamed286@gmail.com

DOI: 10.31838/ecb/2023.12.9.177

INTRODUCTION

Chronic kidney disease (CKD) is a clinical syndrome characterised by a gradual loss of kidney function over time. In particular, the Kidney Disease Improving Global Outcomes (KDIGO) guidelines have defined CKD as abnormalities of kidney structure or function, present for more than 3 months, with implications for health (**1**).

The National Kidney Foundation Kidney Disease Outcomes Quality Initiative (NKF-KDOQI) stages CKD as follows: Stage 1, normal or increased GFR with evidence of kidney damage; stage 2, GFR 60 to 89 ml/min per 1.73 m2; stage 3, GFR 30 to 59 ml/min per 1.73 m2; stage 4, GFR 15 to 29 ml/min per 1.73 m2; stage 5, GFR 15 ml/min per 1.73 m2 or on dialysis (**2**).

Chronic kidney disease (CKD) has become an important public health problem. The primary cause of CKD in children is complex, but when it develops to a certain stage, its pathological changes tend to be the same, such as glomerulosclerosis, interstitial fibrosis, vascular atrophy and collapse, etc. The gross anatomy of these pathological changes mainly shows that the tissue becomes hard (**3**).

Doppler ultrasound may be crucial in determining CKD and how it develops into ESRD. Renal resistive index(RRI) has been found to have a stronger correlation with tubulointerstitial lesions, glomerulosclerosis, and arteriolosclerosis than it does with other morphological factors like renal length and cortical area. Patients with higher RRIs (>0.7) typically exhibit more severe arteriolosclerosis than those with normal or high RRIs (>0.65). RRI >0.7 patients did not respond as well to steroid medication as patients with high-Normal RRI, suggesting that it may be a valuable measure for predicting response (**4**).

The resistive index (RI) is a parameter that indicates the intra-renal arterial resistance. Resistive index is elevated in a variety of kidney diseases, and some studies suggest that RI is related to renal function and patient prognosis **(5).**

The RI values for CKD can be summed up as follows: anticipate response to immunological and hypertensive therapy, estimate renal lesions (vascular, glomerular, and tubulointerstitial), and predict CKD outcome in mild to moderate renal dysfunction (6).

The role of the resistive index as a non-invasive marker for predicting renal pathology in children with CKD. From all Doppler ultrasound indices, the renal resistive index "which is considered a reflection of renal parenchymal resistance" was the best marker of CKD stages. RRI is significantly higher in CKD patients compared to normal control ones and the optimum range of the resistive index is 0.5 to 0.7 **(7).**

PATIENTS AND METHODS

This is a cross-sectional study that was conducted on 58 cases who had CKD stages 3,4,5 in the period starting from January 2021 to September 2022 at the Radiology Department in collaboration with the Nephrology department at Cairo University children's hospital.

Inclusion criteria:

- Age: from 6-13 years.
- All sex.
- Pediatric patients diagnosed with chronic kidney disease (stage 3, 4, 5)
- Control group matched age and sex with normal kidney function tests.

Exclusion criteria:

- Patients with thin renal parenchyma detected by ultrasound.
- Clinically unstable patients.
- Patients with polycystic kidney disease.
- Patients with medullary cystic disease, medullary sponge kidney and nephrolithiasis.
- Patients with renal vein thrombosis, renal artery thrombosis and renal masses.
- Patients refused to participate in the study.

The patients were categorized into three groups:

- **Group A (n = 19)**: Stage 3 CKD with eGFR of 30-59 ml/min/1.73m2.
- **Group B (n = 18):** Stage 4 CKD with eGFR of 15-29 ml/min/1.73m2.
- **Group C (n = 21):** Stage 5 CKD with eGFR of 15 ml/min/1.73m2.

The participants underwent the following steps:

- **GFR estimation**
  - GFR was estimated using standard Schwartz formula eGFR = K× height/ SCr, eGFR is estimated GFR in milliliters per minute per 1.73 m2, height is in centimeters, SCr is serum creatinine in milligram per deciliter, and K is an empirical constant determined by comparing the height/SCr ratio against measured GFR. The value of K is 0.55 for children and adolescent girls, and 0.7 for adolescent boys **(8).**
- **Doppler ultrasonography:**
  - Color doppler imaging was used to asses renal blood flow velocity.
  - All participants were scanned in lying down on the left lateral position then on the right lateral position or a supine or decubitus position to achieve accurate scan as much as possible.
  - This ultrasound was performed for CKD group. Doppler signals were in general obtained from renal artery lying between the superior mesenteric artery and the corresponding renal vein.
  - The resistive index (RI) for each vessel was calculated as an average value obtained from three to five wave forms. After the measurements of homodynamic parameters such as PSV and EDV, the resistive index (RI) was calculated by this equation:
  - RI = (PSV-EDV)/ PS

RESULTS

- This study included 58 patients , 29(50%) were females and 29(50%) were males.Their mean age was 9.3 +_2.43 years. The mean eGFR was (25.75±16.99). 19 patients had CKD stage 3 with eGFR of 30-59 ml/min/1.73m2.18 patients had CKD stage 4 with eGFR of 15-29 ml/min/1.73m2 and 21 patients had CKD stage 5 with eGFR less than 15 ml/min/1.73m2. Different aetiologies of the primary renal disease of the study group is demonstrated in **Figure 1**.

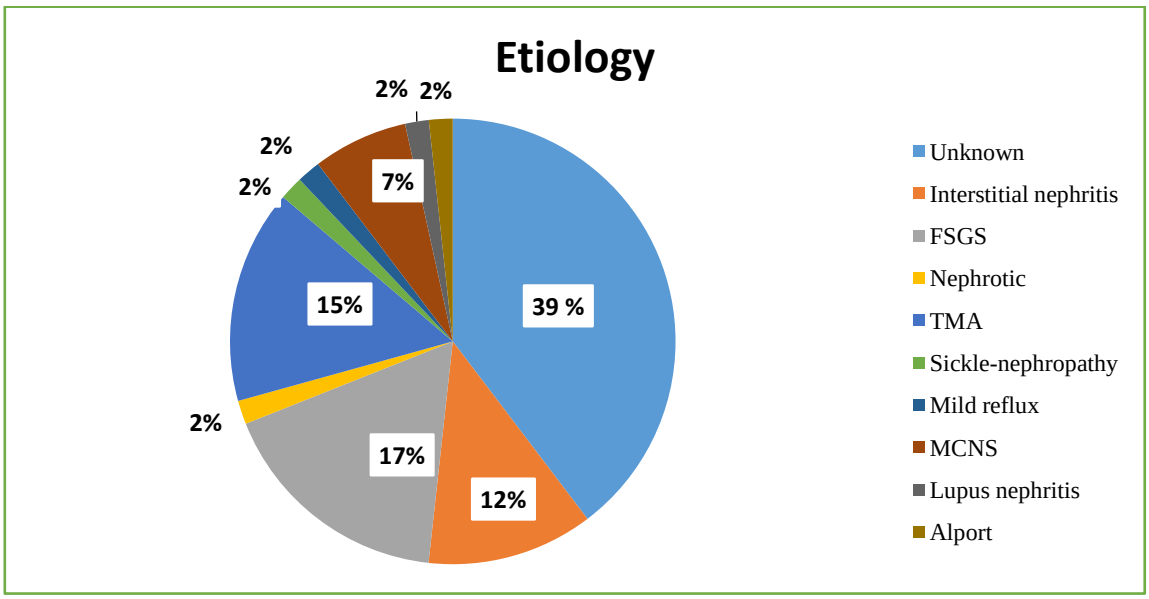

Figure 1: Etiology among CKD group.

Among the cases group, the RI of the right kidney ranged from 0.46-0.87 with a mean 0.59±0.13, while RI of the left kidney ranged from 0.44-0.82 with a mean 0.61±0.09**.**

Correlations between Resistive index and CKD stages were demonstrated in **Table 1**. The RI of the right kidney was significantly increased gradually with the CKD stages. It was significantly higher among stage 5 (0.65±0.10) than Stage 3 (0.54±0.15) and Stage 4 (0.58±0.11) (p=0.044) as shown in **Figure 2.** the RI of left kidney was increased in stage 5 compared to stages 3 and 4, but the difference between them did not reach a significant level (p=0.227).

Table 1:Correlation between Resistive index and CKD stages.

CKD stage	Stage 3 (N=19)	Stage 4 (N=18)	Stage 5 (N=21)	K	P value
RK RI Mean ± SD Range	0.54±0.15 0.0-0.72	0.58±0.11 0.43-0.79	0.65±0.10 0.50-0.87	3.31	**0.044***
Post hock	P1=0.32, **P2=0.013*,** P3=0.159				
LK RI Mean ± SD Range	0.57±0.08 0.44-0.71	0.61±0.097 0.52-0.82	0.62±0.091 0.48-0.80	1.52	**0.227**
Post hock	P1=0.218, P2=1.00, P3=0.750				

RKRI: Right kidney resistive index, **LKRI:** left kidney resistive index
K: Kruskal Wallis test.

P1: stage 3 compared stage 4.
P2: stage 3 compared stage 5.
P3: stage 4 compared stage 5.

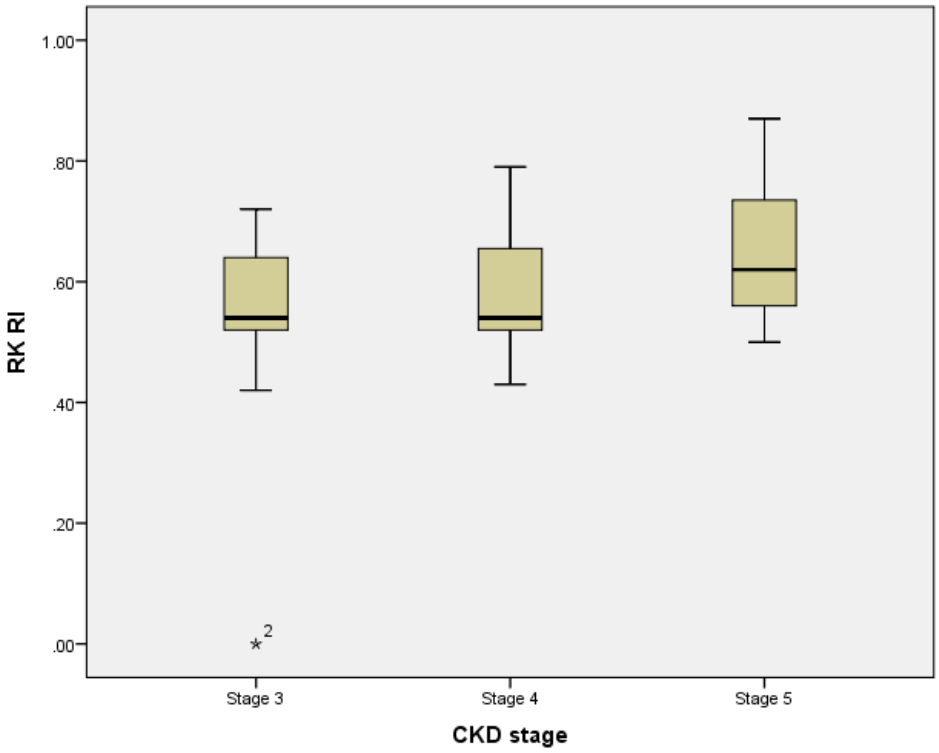

Figure 2. Right kidney resistive index among CKD group.

DISCUSSION

Chronic kidney disease (CKD) has emerged as a significant issue for public health **(9).** Anomalies in renal tubulointerstitial function, glomerular function, and renal vascular function are all directly associated with the development of CKD. Cardiovascular problems are the primary cause of death and disability in children **(10).** It has become a disease of greater concern in the medical community as a result of its increasing incidence and younger patient population, which gravely endangers human health **(11).**

Although the underlying aetiology of CKD in children is complicated, once it reaches a certain stage, its pathological changes, such as glomerulosclerosis, interstitial fibrosis, vascular atrophy and collapse, etc., tend to be consistent. The gross anatomy of these pathological changes mainly shows that the tissue becomes hard. Renal biopsy is the gold standard for diagnosing CKD in the traditional examination; however, due to its invasive nature and difficulty of reuse, it is difficult to use as a general clinical survey or routine means. However, traditional ultrasound technologies can only show positive results when the renal function is obviously damaged **(12).**

The objective of this study was to evaluate the role of resistive index as non-invasive marker for predicting CKD stage in children with chronic kidney disease. From all Doppler ultrasound indices, renal resistive index "which is considered a reflection of renal parenchymal resistance" was the best marker of CKD stages.

In our study, we measured the RI of renal artery for each kidney for all cases of CKD. We found that the RI of the right kidney was significantly increased gradually with CKD stages. It was significantly higher in stage 5 (0.65±0.10) than in stage 3 (0.54±0.15) and stage 4 (0.58±0.11), (p=0.044). The RI of the left of kidney was increased in stage 5 compared to stages 3 and 4, yet with no statistical significance difference. (p = 0.227). As matched with our findings, **Ikee et al.** (7) reported that the optimum range of resistive index is 0.5 to 0.7. On the other hand, others reported that increased RI may not always be a result of renal dysfunction, it may affected by many cardiovascular factors such as vascular compliance, pulsatility index and heart rate (13). Our results indicated that RI was increased with the progression of CKD stage, these findings are inconsistent with previous studies (14, 15, 16). These results may be explained by the fact that, progressive chronic renal disease is believed to reflect a nonspecific renal scarring process involving all renal components, this process results in a reduction in the number and area of post glomerular capillaries. Renal scarring ultimately leads to a reduction in the intrarenal vessel area, which in turn may be responsible for an increased intrarenal vascular resistance. The same findings were found in a study by **Bige et al.** (17).

CONCLUSION

Renal Doppler is a feasible non-invasive technique to assess renal parenchymal resistance in children. It can be used for monitoring of CKD progression.
Resistive index value is related to the progress of kidney dysfunction .With increase of CKD stage, the degree of renal damage gradually progresses, the renal parenchymal resistance gradually progresses, and the resistive index value increases.

REFERENCES

1. **Becherucci, Francesca, Rosa Maria Roperto, Marco Materassi, and Paola Romagnani**. 2016. "Chronic Kidney Disease in Children." Clinical Kidney Journal 9 (4): 583–91. doi:10.1093/ckj/sfw047.
2. **Fadrowski, Jeffrey J, Christopher B Pierce, Stephen R Cole, Marva Moxey-Mims, Bradley A Warady, and Susan L Furth.** 2008. "Hemoglobin Decline in Children with Chronic Kidney Disease: Baseline Results from the chronic kidney disease in Children Prospective Cohort Study." Clinical Journal of the American Society of Nephrology 3 (2): 457–62. doi:10.2215/CJN.03020707.
3. **Liu, Qin, and Zhengrong Wang**. 2021. "Diagnostic Value of Real-Time Shear Wave Elastography in Children with Chronic Kidney Disease." Clinical Hemorheology and Microcirculation 77 (3): 287–93. doi:10.3233/ch-200982.
4. **Hanamura, Kikuno, Akihiro Tojo, Satoshi Kinugasa, Kensuke Asaba, and Toshiro Fujita.** 2012. "The Resistive Index Is a Marker of Renal Function, Pathology, Prognosis, and Responsiveness to Steroid Therapy in Chronic Kidney Disease Patients." International Journal of Nephrology: 139565: 1–9. doi:10.1155/2012/139565.
5. **Swelam, Salwa Hussein, Mohammed Hashim Mahgoob, Mostafa Mohammed Elian, and Mariana Fathy Gayyed**. 2020. "Value of Doppler Ultrasonography in Predicting Renal Pathology in Children with Chronic Kidney Disease." *Current Pediatric Research* 24 (1): 156–60.
6. **Andrikou, Ioannis, Costas Tsioufis, Dimitris Konstantinidis, Alexandros Kasiakogias, Kyriakos Dimitriadis, Ioannis Leontsinis, Eirini Andrikou, Elias Sanidas, Ioannis Kallikazaros, and Dimitris Tousoulis**. 2018. "Renal Resistive Index in Hypertensive Patients." Journal of Clinical Hypertension (Greenwich, Conn.) 20 (12). John Wiley and Sons Inc.: 1739–44. doi:10.1111/jch.13410.
7. **Ikee, Ryota, Shuzo Kobayashi, Noriaki Hemmi, Toshihiko Imakiire, Yuichi Kikuchi, Hidekazu Moriya, Shigenobu Suzuki, and Soichiro Miura.** 2005. "Correlation Between the Resistive Index by Doppler Ultrasound and Kidney Function and Histology." American Journal of Kidney Diseases 46 (4): 603–9. doi: 10.1053/j.ajkd.2005.06.006.
8. **Schwartz, George J, and Dana F Work**. 2009. "Measurement and Estimation of GFR in Children and Adolescents." Clinical Journal of the American Society of Nephrology 4 (11): 1832–43. doi:10.2215/cjn.01640309.
9. **Zhang, Luxia, Fang Wang, Li Wang, Wenke Wang, Bicheng Liu, Jian Liu, Menghua Chen, et al**. 2012. "Prevalence of Chronic Kidney Disease in China: A Cross-Sectional Survey." The Lancet 379 (9818): 815–22. doi:10.1016/s0140-6736(12)60033-6.
10. **Ruiz-Ortega, Marta, Sandra Rayego-Mateos, Santiago Lamas, Alberto Ortiz, and Raul R Rodrigues-Diez**. 2020. "Targeting the Progression of Chronic Kidney Disease." Nature Reviews Nephrology 16 (5): 269–88. doi:10.1038/s41581-019-0248-y.
11. **Zhang, Jie, Cuirong Duan, Xingxing Duan, Yuan Hu, Jinqiao Liu, and Wenjuan Chen**. 2022. "Quantitative Evaluation of Real-Time Shear-Wave Elastography under Deep Learning in Children with Chronic Kidney Disease.". Hindawi Limited: 1–9. doi:10.1155/2022/6051695.
12. **Liu, Qin, and Zhengrong Wang**. 2021. "Diagnostic Value of Real-Time Shear Wave Elastography in Children with Chronic Kidney Disease." Clinical Hemorheology and Microcirculation 77 (3): 287–93. doi:10.3233/ch-200982.
13. **Watanabe S, Okura T, Kurata M, Irita J, Manabe S, Miyoshi K, Fukuoka T, Gotoh A, Uchida K, Higaki J.**2006. ''Valsartan reduces serum cystatin C and the renal vascular resistance in patients with essential hypertension.'' Clin Exp Hypertens 28(5):451-61.
14. **Asaba K, Tojo A, Onozato ML, Kinugasa S, Miyazaki H, Miyashita K, Uehara Y, Hirata Y, Kimura K, Goto A, Omata M and Fujita T.**2009. '' Long-term renal prognosis of IgA nephropathy with therapeutic trend shifts." Intern Med; 48:883-90.
15. **Petersen LJ, Petersen JR. Talleruphuus U, Ladefoged SD, Mehlsen J, Jensen HA.** 1997." The pulsatility index and the resistive index in renal arteries. Associations with long-term progression in chronic renal failure. " Nephrology Dialysis Transplantation 12(7):1376- 80.
16. **Hanamura K, Akihiro T, Satoshi K, Kensuke A, Toshiro F.** 2012.'' The Resistive Index Is a Marker of Renal Function, Pathology, Prognosis, and Responsiveness to Steroid Therapy in Chronic Kidney Disease Patients. " Int J Nephrol. 2012: 139565.
17. **Bigé N, Lévy PP, Callard P, Faintuch JM, Chigot V, Jousselin V, Ronco P, Boffa JJ.** 2012 . '' Renal arterial resistive index is associated with severe histological changes and poor renal outcome during chronic kidney disease. " BMC Nephrol. 25; 13: 139. doi: 10.1186/1471-2369-13-139.