Section: Radiodiagnosis

Original Research Article

TO STUDY THE CORRELATION OF APPARENT DIFFUSION COEFFICIENT (ADC) VALUES OF RENAL PARENCHYMA AND RENAL RESISTIVE INDEX (RRI) WITH SERUM MARKERS OF RENAL DYSFUNCTION AND STAGE OF CHRONIC KIDNEY DISEASE

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ABSTRACT

Background: The objective was to investigate the correlation between ADC values of DW-MRI and Renal Resistivity Index (RI)of the renal parenchyma in assessing various stages of chronic kidney disease.

Materials and Methods: It is a single institutional prospective study in Govt General hospital, Kurnool. Approval got from by institutional ethical committee. The informed consent from the patients and controls have been obtained Patients who came for MRI abdomen and spine both non renal and the renal disorder and to renal Doppler study with normal and elevated renal parameters were identified and included in the study.

Results: In our study, there has been steady decreasing trend in ADC values with the decrease in eGFRi .e., with the progression of severity(stage) of CKD. The level of serum creatinine and the stage of chronic kidney disease are inversely correlated with the ADC value, which also demonstrated a decreasing tendency. In conclusion, RI $\geq$ 0.79 on the renal duplex ultrasonography can be a helpful predictor for renal progression in patients with moderate renal dysfunction, regardless of their ACE inhibitors and ARB as angiotensin receptor blockers usage. Therefore, checking the RI value is helpful when we evaluate kidney ultrasonography in patients with moderate renal dysfunction.

Conclusion: The value of the apparent diffusion coefficient can be used as an extra marker to determine the level of renal function. ADC can be used to determine the degree of renal impairment. ADC values continues to decrease with increase in severity (stage) of chronic kidney disease. DWI is recognized as a promising imaging tool that can take part in the assessment of the morphological and functional changes in diffuse renal parenchymal disease, hence playing an important role in the early diagnosis and staging of chronic kidney disease.

Keywords: ADC, Chronic Kidney disease, MRI, GFR, Creatinine.

INTRODUCTION

Chronic Kidney Disease (CKD) is a significant global health concern which is associated with an increased risk of multiple organ failure it can be a devastating illness with numerous life-long consequences

End-stage renal disease affects 100–150 people per million people worldwide, making chronic renal illness a major public health concern.

Renal dysfunction: Is a Condition defined according to the presence or absence of damage of the kidneys and level of kidney function, not related to the type of kidney damage

Many individuals with impaired renal function also have a kidney disease, which will get worse over time. When kidney function drops below 25%, a number of health issues start to appear. People are unable to survive for very long without renal replacement therapy, such as dialysis or transplantation, when their glomerular filtration rate (GFR) falls below 15%. The kidneys become unable to eliminate enough creatinine and excess water from the blood if the GFR is too low. The estimation of creatinine in the blood can be used to determine eGFR indirectly. The breakdown of healthy muscle cells produces creatinine. Therefore, the level of renal function is correlated with the serum creatinine level.[1-4]

Renal dysfunction is determined by either absence / decrease in the production of urine or elevation in the waste products (serum Creatinine / blood Urea) level in the blood. Pathology involving the renal parenchyma will leads to renal dysfunction. Monitoring of the renal function will provide degree of progression of dysfunction. The regular assessment of renal-function is ideal for treatment in renal disease.[5]

Blood urea, serum creatinine, and eGFR are indirect measures of renal function that do not account for the individual functions of each kidney.

Due to the limits of serum indicators, imaging plays a significant role in the evaluation of renal parenchymal disease.

Imaging investigations give information on the anatomy and function of each kidney individually.

Imaging techniques

- Plain radiography
- Conventional urography
- Ultra sonogram with Doppler
- CT urography
- MRI
- Radio nucleotide imaging

Aims & Objectives

The objective was to investigate the correlation between ADC values of DW-MRI and Renal Resistivity Index (RI) of the renal parenchyma in assessing various stages of chronic kidney disease.

MATERIAL AND METHODS

Design of study

- Prospective observational study
- Sample size- 50patients
- Study period-6 months
- Study centre- Government General Hospital, Kurnool medical college, kurnool

Inclusion Criteria

- Patients who has elevated renal parameters Serum creatinine>1.5mg/dl, Blood urea >40mg/dl
- Patients with normal renal parameters but more risk factors

Exclusion Criteria

- Non consenting patient
- Patient who cannot breath hold

Duration of Study: 6 months (May 2022 –October 2022)

Method of Collection of Data Study

It is a single institutional prospective study in Govt General hospital, KURNOOL. Approval got from by institutional ethical committee. The informed consent from the patients and controls have been obtained Patients who came for MRI abdomen and spine both non renal and the renal disorder and to renal Doppler study with normal and elevated renal parameters were identified and included in the study. Diffusion weighted imaging and Renal Doppler study was performed of all patients with elevated renal parameters and in patients with normal renal parameters.

The cases are divided based on the presence of renal dysfunction, with cut off value for Serum Creatinine (sr.cr)> 1.5 mg/dl. Totally 50 patients with both renal dysfunction and normal serum renal parameters were identified. Mean Creatinine Level for group with the renal dysfunction group was 3.2 mg/dl (range 1.6-15.4 mg/dl) and mean Blood Urea was 63.9 mg/dl (range 30-156 mg/dl). We have not selected the patients as acute and chronic kidney disease as separate entity.

Patients were classified into stages based on the disease severity, as per the level of serum creatinine and blood urea level. Data including age, sex, clinical, and laboratory parameters were collected. eGFR was calculated by using CKD EPI Formula. We selected the patients only based on theelevated renal parameters.

RESULTS

Patient characteristics

The population of our study 50 patients (men, women, mean age 39.5 years), 20 females, 30 male patients.

Table showing the age distribution. Mean age of the study subjects is 45.58 + 11.67. Most (32%) of the study subjects are in the age group of 41-50 years .24% are in the age group of 51-60 years. 22% are in the age group of 31-40 years. 12% are in the age group of 21-30 years and 10% are in the age group of > 60 years. [Table 1]

Table 2: Showing the age and sex distribution. Majority of the males are in the age group of 41-50 years. Females are majority in age group of 31-40 years. [Table 2]

Table 3: Showing the blood urea. Majority i.e 68% are having abnormal blood urea and 32% are having blood urea in normal range. [Table 3]

Table 4: Showing the serum creatinine .42% of the patients are having abnormal creatinine value > 1.5 mg/dl, whereas 42% of them are having normal creatinine values. [Table 4]

Table 5 Urea v/s ADC. Mean ADC value is 2.4 on both sides in normal urea patients and it is 2 on both sides in abnormal urea patients. [Table 5]

Table 6: Showing urea v/s RI. Mean RI value is 0.64 on both sides in normal urea patients and it is 0.65 on right side and 0.66 on left side in abnormal urea patients. [Table 6]

Table 7; Showing creatinine v/s ADC. Mean ADC value is 2.38 on right side and 2.35 on left side in normal creatinine patients. Mean ADC on right side is 1.86 on right side and 1.78 on left side in abnormal creatinine patients. [Table 7]

TABLE 8: Showing CREATININE V/S RI. Mean RI value on right side is 0.63 and,on left side is 0.64 in normal creatinine patients. Mean value of RI is 0.69 on right side and 0.67 on left side in abnormal creatinine patients. [Table 8]

Table 9: Showing creatine v/s ADC. Mean ADC up to 1.5 mg/dl of creatinine is 2.38 on right side and 2.35 on left side. Mean ADC from 1.6-5 mg/dl is 1.94 on right side and 1.87 on left side. Mean ADC above 5 mg/dl is 1.69 on right side and 1.58 on left side. [Table 9]

More than 90 ml/min/1.73m^2 is taken as normal eGFR. Less than this is considered as abnormal.

Table 10: Showing GFR.74% of the patients had abnormal GFR and 26% had normal GFR. [Table 10]

Table 11: Showing creatinine v/s eGFR. 13 patients had normal eGFR and serum creatinine. 14 patients had abnormal eGFR and normal creatinine. 23 patients had abnormal eGFR and abnormal creatinine. [Table 11]

TABLE 12. Showing the correlation between RI & GFR.

There is negative correlation between eGFR and RI.

Representative Cases

Patient name: RANGAIAH M/55 yrs

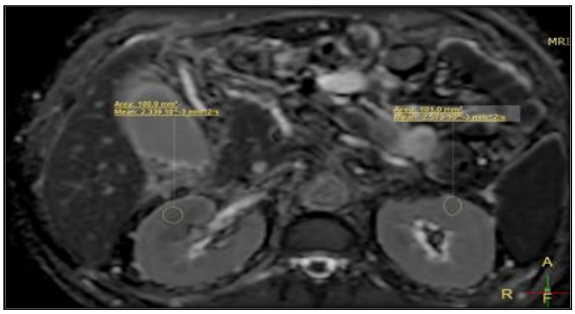

Figure 1. MRI DWI image showing ADC values
ADC Rt-2.33 Lt-2.57

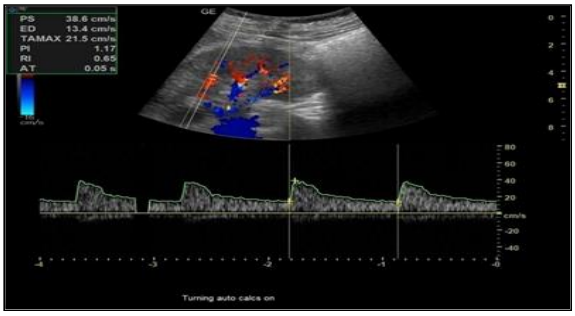

Figure 2: RI-0.65: Doppler image displaying wave pattern and different Doppler indices Patient name; SHABEERA BEGUM F/35 yrs

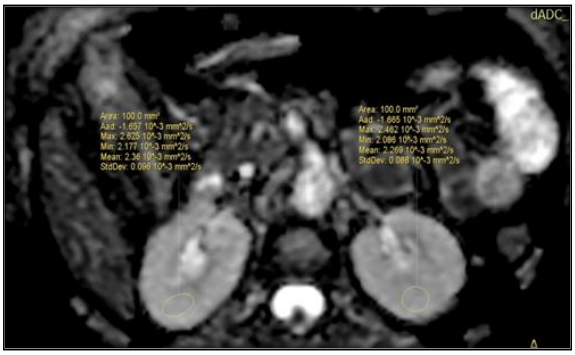

Figure 3. MRI DWI image showing ADC values
ADC - Rt-2.36 Left-2.26

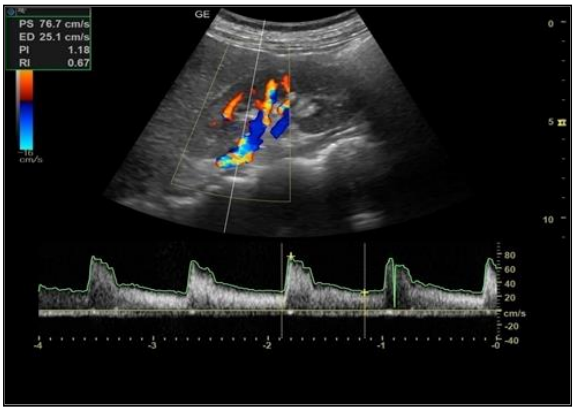

Figure 4: RI- 0.67Doppler image

Table 13: Showing the mean of of the ADC on right and left side which is showing the decreasing trend. As the stage of CKD is progressing ADC value is decreasing. [Table 13]

Table 14: Showing the correlation between urea, creatinine v/s ADC. [Table 14]

There is negative correlation between urea and ADC on right and left side and so is the creatinine with ADC. The ADC value will drop as serum creatinine levels rise. Only patients with significantly increased creatinine levels and those with stage 4, 5 CKD will have very low levels of ADC. In individuals with renal failure, the relationship between renal parenchymal ADC values and glomerular filtration rate is positive and linear. Those with normal GFR will see high ADC readings. The mean ADC values of the various creatinine groups varied greatly from one another.

The level of serum creatinine and the stage of chronic kidney disease are inversely correlated with the ADC value, which also demonstrated a decreasing tendency.

Low ADC levels are statistically significant as chronic renal disease progresses. In order to assess and track the level of renal impairment, the ADC values might be added in addition.

If the baseline ADC values are fixed, it will be possible to track the development of parenchymal illness in a manner similar to how serum creatinine levels are monitored. Cut-offs can be defined for ADC values to distinguish between different CKD stages. As a result, we can evaluate the ADC values

of the individual kidneys to determine whether they are functioning properly.

When measured in the cystic areas, ADC values for cystic renal disease were high. Therefore, measurements of ADC were made on patients who had renal cysts outside of those locations. To become an accepted clinical tool, improvement in DWI reliability and homogenization of acquisition techniques in multicentre studies are crucial.

Table 1: Age Distribution

AGE RANGE (years)	NO.OF PATIENTS (n)	PERCENTAGE
21-30	6	12%
31-40	11	22%
41-50	16	32%
51-60	12	24%
>60	5	10%

Table 2: Age and Sex Distribution

AGE	MALE	FEMALE
21-30 YEARS	2	4
31-40 YEARS	4	7
41-50 YEARS	12	4
51-60 YEARS	8	4
>60 YEARS	4	1

Table 3: Blood Urea

BLOOD UREA	NO.OF PATIENTS	MEAN	SD	P VALUE
NORMAL (<40 mg/dl)	16 (32%)	35	3.4	0.001
ABNORMAL (>40mg/dl)	34 (68%)	63	30.2	0.001

Table 4: Serum Creatinine

SERUM CREATININE	NO.OF PATIENTS	MEAN	SD	PVALUE
NORMAL(<1.4mg/dl)	29 (58%)	1.038	0.26	0.001
ABNORMAL(>1.5mg/dl)	21 (42%)	4.77	3.76	0.001

Table 5: Urea v/s ADC

UREA	ADC(RT)	ADC(LT)	P VALUE
NORMAL	2.44	2.4	0.001
ABNORMAL	2.05	2	0.001

Table 6: Urea V/S RI

UREA	RI (RT)	RI (LT)	P VALUE
NORMAL	0.64	0.64	0.001
ABNORMAL	0.65	0.66	0.001

Table 7: Creatinine v/s ADC

CREATININE	ADC(RT)	ADC (LT)	P VALUE
NORMAL	2.38	2.35	0.001
ABNORMAL	1.86	1.78	0.001

Table 8: Creatinine v/s RI

CREATININE	RI (RT)	RI (LT)	P VALUE
NORMAL	0.63	0.64	0.001
ABNORMAL	0.69	0.67	0.001

Table 9: Creatinine Range V/S ADC

CREATININE	ADC (RT)	ADC (LT)	P VALUE
UPTO 1.5mg/dl	2.38	2.35	0.001
1.6-5 mg/dl	1.94	1.87	0.001
ABOVE 5 mg/dl	1.69	1.58	0.001

Table 10: GFR

GFR	NO.OF PATIENTS	PERCENTAGE	MEAN	SD	P VALUE
NORMAL	13	26%			
ABNORMAL	37	74%	58.36	38.59	0.001

Table 11: Creatinine v/s GFR

CREATININE	GFR (N)	GFR(AB)
NORMAL	13	14

ABNORMAL	0	23

Table 12: Correlation Between RI & GFR

	RI(RT)	RI(LT)
GFR	-0.26	-0.35
P VALUE	0.06	0.01

Table 13: Stages of CKD v/s ADC

STAGE OF CKD	ADC (RT)	ADC(LT)	P VALUE
STAGE I	2.47	2.39	0.001
STAGE II	2.36	2.35	0.001
STAGE III	1.96	2.04	0.001
STAGEIV	1.98	1.72	0.001
STAGE V	1.69	1.58	0.001

Table 14: Correlation Between Urea, Creatinine V/S ADC

	ADC(RT) (r)	ADC(LT) (r)	P VALUE
UREA	-0.65	-0.68	0.001
CREATININE	-0.56	-0.61	0.001

DISCUSSION

When compared to patients with normal renal serum indicators, patients with higher renal parameters had considerably lower levels of ADC in their renal parenchyma.

Reduced perfusion and reduced water diffusion are likely to be the cause of lower ADC values in renal parenchymal disease, which increases blood urea and serum creatinine.

Glomerulo-sclerosis, tubular atrophy, and interstitial fibrosis all result in reduced levels of ADC because there is less free mobility of water molecules both inside and outside of cells.

Study by Doaa et al titled "Role of diffusion-weighted magnetic resonance imaging in evaluation of chronic kidney disease"had found that there was a significant relationship between the ADC values and GFR, as the ADC values of CKD kidneys were significantly lower than normal kidneys, and the mean ADC values of different CKD stages were significantly different from each other and showed a decreasing trend with increasing stage.

In our study, there has been steady decreasing trend in ADC values with the decrease in eGFR i.e., with the progression of severity(stage) of CKD. Study by Haramb at J et al,[6] had found that DWI is recognized as a powerful imaging biomarker of the renal microstructure with a number of available clinical studies. DWI shows good correlation with renal function decline and with cortical fibrosis in CKD, with a promising monitoring potential.

Resistive Indexvs Serum Creatinine/ Blood urea:

RI of the kidneys were compared with the serum markers of renal function.

In a study by Kocyigita A et al,[7] which study subjects were selected who are planned for renal biopsy in search of a definitive histopathological evidence of underlying disease, Concluded that sonographic and Doppler parameters are helpful in predicting different stages of CKD in children. Any increase in the RI and PI values must arouse alarm to the possibility of advancing renal damage. Moreover, RI and PI could fairly predict the degree of glomerular sclerosis and interstitial fibrosis.[5] Study by Yildirim E et al,[8]found that RI is higher in CKD patients with CVD, diabetes, smoking habit and higher serum phosphorus, regardless of eGFR.[3]

Mean RI levels were also higher in patients with a history of previous CVD, smoking habit and in the presence of diabetes. US-Doppler imaging has already been defined as a reliable tool for assessing the severity of CKD. The advantages of this method are represented by its ability to detect macroscopic vascular abnormalities in the kidney and to provide important diagnostic and prognostic information.

Moreover, the increasing use of RI as a predictor of bad outcomes in CKD patients, such as the eGFR decline, encourages a more detailed investigation of the clinical parameters that may be associated with a worsening of US metrics. Further studies are needed to verify whether higher RI indicates more complex pathway of intra renal damage, besides and beyond kidney function.

A study by Zheng Z et al,[9] showed that the patients with RI $\geq$ 0.79 had significantly higher incidence of renal progression than those with RI < 0.796Another previous study showed Yoshikawa T et al,[10] that RI > 0.8 on renal duplex ultrasonography was a predictor of worsened renal function and progression to renal replacement in patients newly diagnosed with CKDIn conclusion, RI $\geq$ 0.79 on the renal duplex ultrasonography can be a helpful predictor for renal progression in patients with moderate renal dysfunction, regardless of their ACEI or ARB usage. Therefore, checking the RI value is helpful when we evaluate kidney ultrasonography in patients with moderate renal dysfunction.

RI values cannot be reliably correlated with the serum creatinine level. Measuring the RI value perfectly in patients the severely contracted kidneys and those unable to hold breath is difficult which operator dependent and needs patient co-operation. And some cases measuring RI is very difficult (obese

persons, severely contracted kidneys, patients who unable to hold breath). Patients with renal dysfunction varied RI values from 0.54to 0.78. (p value>0.05)

Renal Resistive Index vs ADC

RI values of all the patients normal and abnormal parameters were collected. Comparing the RI value with ADC values patients with normal renal parameters shown normal RI Values. Those with deranged renal parameters shown variable RI values and not correlating with the elevated renal parameters as like ADC values (P value>0.05).It is due to rise in the RI value in renal dysfunction patient depends on pathology (tubulo interstitial/glomerular). In this study we didn't selected patients with proven pathology .so it is unable to correlate the RI with the cause of pathology

Limitations of the study

- The study group's sample size was small.
- Patients with renal impairment for which there is no known cause.
- There is no established protocol for renal DW-MRI.
- The choice of b values for renal imaging is one of the main restrictions on the widespread adoption of DWI. It will be challenging to establish cut off values because different studies have used different b values.
- Extensive study is required to assess the precision and accuracy of ADC data obtained from various MRI systems. Researchers will be able to confidently use DWI in clinical practise after the study's conclusion and fix ADC Values in a reliable manner.

CONCLUSION

The value of the apparent diffusion coefficient can be used as an extra marker to determine the level of renal function. ADC can be used to determine the degree of renal impairment. ADC values continues to decrease with increase in severity (stage) of chronic kidney disease. When a patient undergoes an MRI and does not previously have renal disease, the Diffusion Weighted Imaging assessment of kidney function will help the doctor decide whether to administer contrast. Cut-off values for the ADC can be established to determine renal impairment and the various phases of CKD. Because the rise in the renal resistive index depends on the pathology (tubulo-interstitial or glomerular), it is not possible to utilise the renal resistive index as a reliable marker to determine the stage of renal disease and the progression of renal dysfunction.

Conflict of Interest: None

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