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ORIGINAL RESEARCH

Assessment of renal ADC values in normal and diabetic patients by DWI MRI sequence

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ABSTRACT

Background: The term "diabetic nephropathy" refers to a clinical syndrome that includes persistent albuminuria, a consistent decrease in glomerular filtration rate (GFR) that eventually leads to end-stage renal disease, elevated arterial blood pressure, and increased cardiovascular morbidity and mortality. The apparent diffusion coefficient (ADC) has shown potential as a marker of renal function in several investigations, with decreased renal ADC in kidney disease. The aim of this study was to assess the difference in apparent diffusion coefficient (ADC) value in normal and diabetic kidney.

Methods: This was a cross sectional analytical study conducted from January 2021 to October 2022 in in Department of Radio diagnosis with the help of Department of Medicine. The cases coming to the Department of Medicine for routine follow up fulfilling the inclusion (age >18 years of diabetes mellitus with history of diabetic nephropathy). The MRI examination was performed using a 3 Tesla system.Binary logistic regression analysis was used for estimating the parameters of a logistic model (the coefficients in the linear combination). The p-value was taken significant when less than 0.05 and confidence interval of 95% was taken.

Results: In the study 26 (52%) cases were of diabetes mellitus while 24 (48%) cases were taken as control who were non diabetic. Out of 26 cases, majority belong to the stage 3 (46.2%) followed by the stage 4 and stage 5 with 6 (23.1%) cases each. The study included 1 case each of Stage 1 and stage 2. The ROC Analysis to find Accuracy of ADC Parameters for Detecting DM revealed that Lt, Rt and overall ADC values are highly accurate for detecting DM cases as their AUROC values comes out to be 0.999, 0.960 and 1.000 respectively, the very close/equal to perfect standard 1.000.

Conclusion: The magnetic resonance imaging- Apparent diffusion Coefficient (ADC) value is an appropriate method for assessment and evaluation of diabetic nephropathy. Renal ADC values show a significant correlation with clinical stages of diabetic nephropathy, it is a reliable diagnostic tool for differentiation between diabetic nephropathy patients from diabetic patients without nephropathy.

Keywords: Diabetes Mellitus, Renal Nephropathy, Magnetic resonance imaging, Apparent diffusion coefficient, Glomerular filtration rate

INTRODUCTION

The term "diabetic nephropathy" refers to a clinical syndrome that includes persistent albuminuria, a consistent decrease in glomerular filtration rate (GFR) that eventually leads to end-stage renal disease, elevated arterial blood pressure, and increased cardiovascular morbidity and mortality (1). Renal functional decline in diabetic patients is caused by a variety of structural changes to the kidneys, such as glomerular basal membrane thickening and mesangial expansion, extracellular matrix buildup, mesangiolysis, a decrease in podocyte number, the development of microaneurysms, and arteriolar hyalinosis, which eventually results in glomerulosclerosis, tubular atrophy, interstitial expansion, and fibrosis (2).

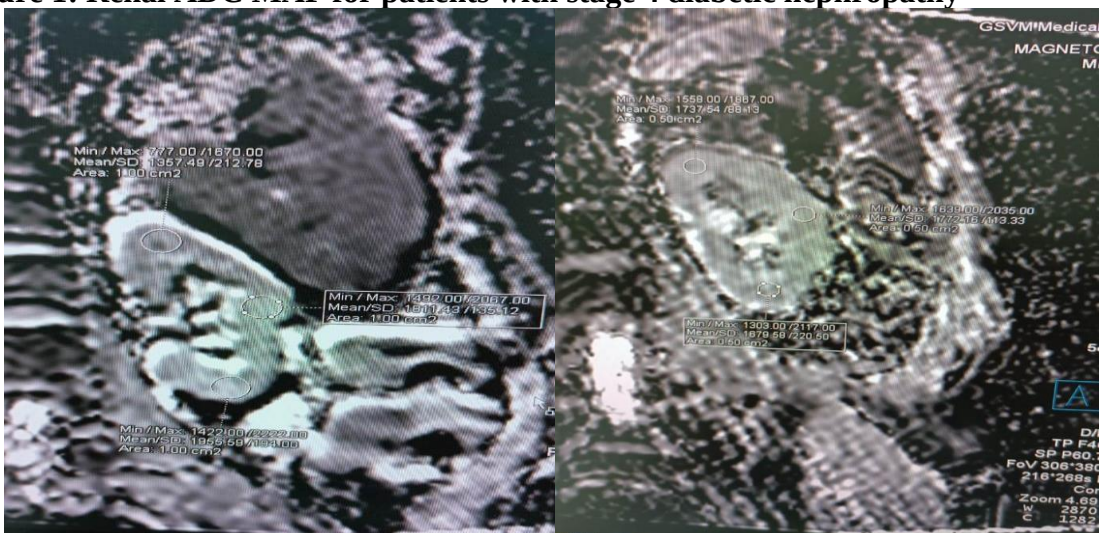
There are various phases of renal injury. Diabetic nephropathy has no symptoms in the early stages. Clinical nephropathy's onset is predicted by persistent microalbuminuria. It has been suggested that microalbuminuria is a sign for extensive endothelial dysfunction and denotes microvascular injury (3). The development of more efficient follow-up and treatment strategies may be facilitated by a better knowledge of the mechanisms that result in structural and functional alterations in the diabetic kidney.

Early detection of microvascular damage by diagnostic testing will be extremely helpful in controlling the condition.This chance may be provided by quantitative diffusion-weighted MRI, which can also be used to assess renal dysfunction. The apparent diffusion coefficient (ADC) has shown potential as a marker of renal function in several investigations, with decreased renal ADC in kidney disease (4,5). However, the utility of renal quantitative diffusion-weighted imaging (DWI) in diabetic nephropathy has only been investigated in a small number of investigations (6,7,8). The aim of this study was to assess the difference in apparent diffusion coefficient (ADC) value in normal and diabetic kidney and assess the correlation between Clinical stages of diabetic nephropathy

MATERIALS AND METHODS

This was a cross sectional analytical study conducted from January 2021 to October 2022 in GSVM Medical College, Kanpur. The study was conducted in Department of Radio diagnosis with the help of Department of Medicine.The cases coming to the Department of Medicine for routine follow up fulfilling the inclusion (age >18 years of diabetes mellitus with history of diabetic nephropathy) and exclusion criteria (any contraindication for MRI [metallic prosthesis, pacemaker, claustrophobia] for MRI, congenital hypoplastic kidney, large cysts (>3cm) or having multiple cysts (>3), obstructive uropathy, pyelonephritis and prior renal surgical history) will be selected and enrolled in the study after taking informed consent.The diabetic patients were classified according to glomerular filtration rate (GFR) into two groups; group I: 26 diabetic patients with nephropathy and group II: 24 non diabetic patients without nephropathy. The investigation included fasting blood sugar and post prandial blood sugar, Kidney function test and HbA1c. The MRI examination was performed using a 3 Tesla system (MAGNETOM Vida, siemens medical system, Germany) (Figure 1).

Figure 1: Renal ADC MAP for patients with stage 4 diabetic nephropathy



STATISTICAL ANALYSIS

The results were analysed using descriptive statistics and making comparisons among the various groups. Categorical data were summarized as in proportions and percentages (%) while discrete in mean and SD. An unpaired t-test was used to compares the means of two groups to determine if there is a significant difference between the two.ROC analysis was used for diagnostic test evaluation where the true positive rate (Sensitivity) was plotted in function of the false positive rate (100-Specificity) for different cut-off points of a parameter.Binary logistic regression analysis was used for estimating the parameters of a logistic model (the coefficients in the linear combination). The p-value was taken significant when less than 0.05 and confidence interval of 95% was taken.

RESULTS

In the study 26 (52%) cases were of diabetes mellitus while 24 (48%) cases were taken as control who were non diabetic.Out of 26 cases, majority belong to the stage 3 (46.2%) followed by the stage 4 and stage 5 with 6 (23.1%) cases each. The study included 1 case each of Stage 1 and stage 2 (Table 1).In the study males were in majority. Out of 50 subjects, 31 (62%) were males and rest 19 (38%) were females.

Table 1: Distribution of study subjects by stage.

Stage	Frequency	%
Stage 1	1	3.8
Stage 2	1	3.8
Stage 3	12	46.2
Stage 4	6	23.1
Stage 5	6	23.1
Total	26	100.0

The mean age of the normal group was 44.46±13.15 year while the mean age of DM group was 53.92±10.80 year. The significant difference was found in mean ages between the groups (p=0.008). The mean height of the normal group was 165.67±5.47 cm while the mean height of DM group was 165.66±6.30 cm. No significant difference was found in mean heights between the groups (p=0.996).The mean weight of the normal group was 66.38±7.94 kg while the mean weight of DM group was 67.23±6.00 kg. No significant difference was found in mean weights between the groups (p=0.666).

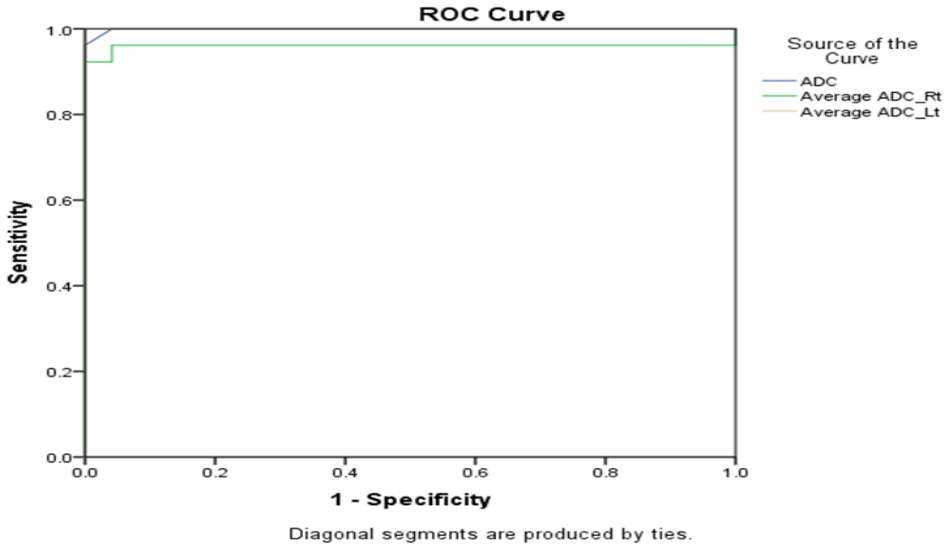
The mean HbA1c of the normal group was 5.59±0.33 while the mean HbA1c of DM group was 7.04±0.31. The significant difference was found in mean HbA1c between the groups (p<0.001).The mean of the Rt Average ADC of the normal group was 2.31±0.05 while the mean of the Rt Average ADC of DM group was 1.86±0.22. The significant difference was found in mean of the Rt Average ADC between the groups (p<0.001). The mean of the Lt Average ADC of the normal group was 2.31±0.04 while the mean of the Rt Average ADC of DM group was 1.85±0.20. The significant difference was found in mean of the Lt Average ADC between the groups (p<0.001). The mean of the Average ADC of the normal group was 2.31±0.03 while the mean of the Average ADC of DM group was 1.86±0.20. The significant difference was found in mean of the Average ADC between the groups (p<0.001) (Table 2).

Table 2: Comparison of kidney function parameters between normal and DM cases

Variable	Normal		DM		unpaired t test	
	Mean	SD	Mean	SD	t-value	p-value
Sugar Fasting (mg/dl)	83.00	5.87	120.12	11.47	14.22	<0.001
Sugar PP(mg/dl)	131.33	13.60	179.35	15.60	11.56	<0.001
HbA1C	5.59	0.33	7.04	0.31	15.99	<0.001
eGFR	114.13	13.11	28.73	16.95	19.80	<0.001
S.Creatinine (mg/dl)	0.79	0.11	2.90	1.21	-8.53	<0.001
Average ADC_Rt	2.31	0.05	1.86	0.22	9.56	<0.001
Average ADC_Lt	2.31	0.04	1.85	0.20	11.33	<0.001
ADC	2.31	0.03	1.86	0.20	10.95	<0.001

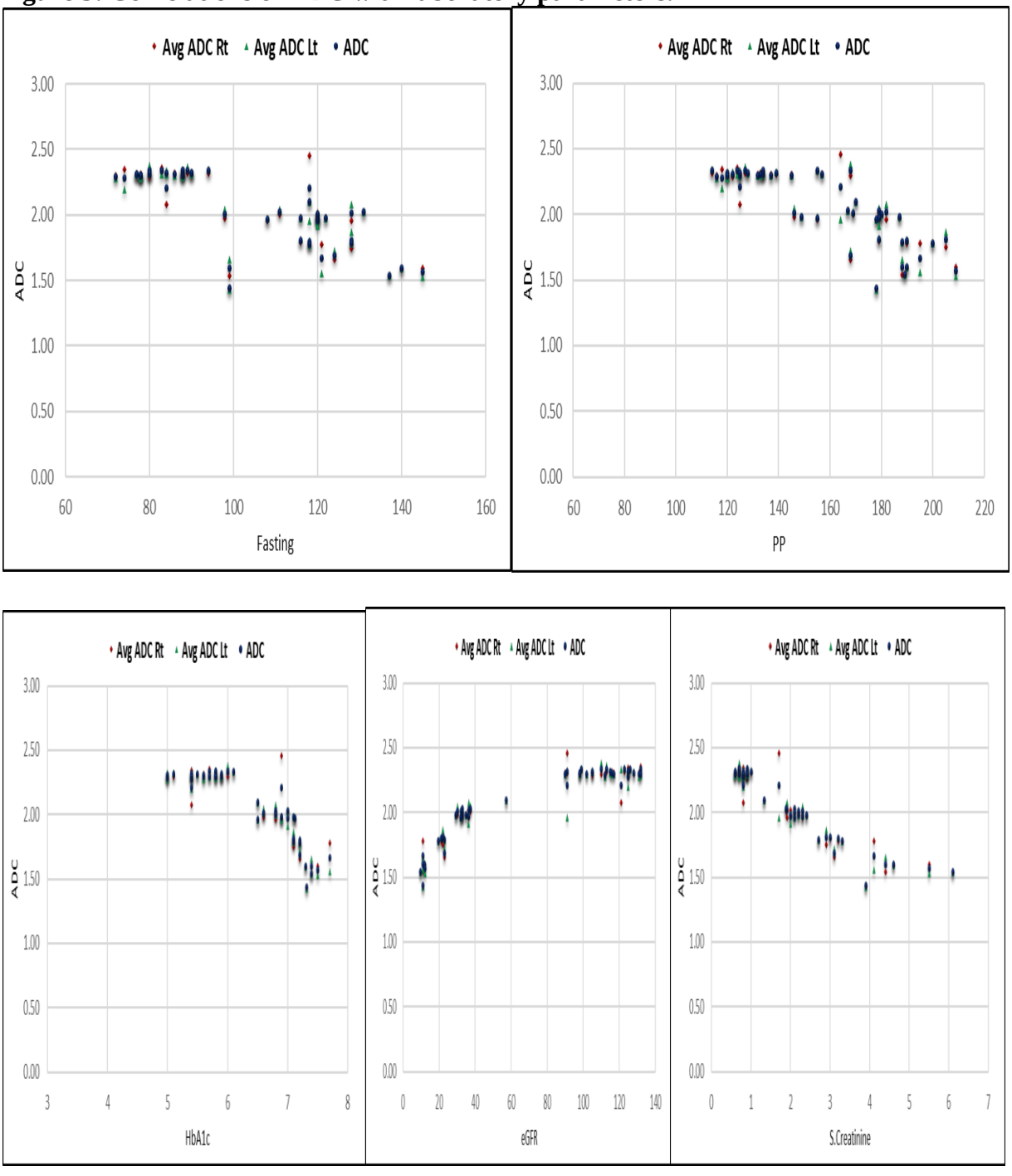
The ROC Analysis to find Accuracy of ADC Parameters for Detecting DM revealed that Lt, Rt and overall ADC values are highly accurate for detecting DM cases as their AUROC values comes out to be 0.999, 0.960 and 1.000 respectively, the very close/equal to perfect standard 1.000. The optimum cut off for detecting DM by ADC values is given as: Rt ADC<2.155, Lt ADC < 2.055 and Overall ADC < 2.150. The cut off of Rt ADC had sensitivity and specificity 96.2% & 100% respectively.The cut off of Lt ADC had sensitivity and specificity 92.2% & 100% respectively.The cut off of overall ADC had sensitivity and specificity 100% & 100% respectively (Figure 2).

Figure 2: ROC analysis to find accuracy of ADC parameters for detecting DM



The average Rt ADC showed significant negative correlations with Fasting BG (r=-0.756, p<0.001), PP BG (r=-0.811, p<0.001), HbA1c (r=-0.844, p<0.001) and Sr Creatinine (r=-0.928, p<0.001) and significant positive correlation with eGFR (r=0.903, p<0.001).The average Lt ADC showed significant negative correlations with Fasting BG (r=-0.798, p<0.001), PP BG (r=-0.831, p<0.001), HbA1c (r=-0.896, p<0.001) and Sr Creatinine (r=-0.953, p<0.001) and significant positive correlation with eGFR (r=0.895, p<0.001).The average ADC showed significant negative correlations with Fasting BG (r=-0.790, p<0.001), PP BG (r=-0.834, p<0.001), HbA1c (r=-0.884, p<0.001) and Sr Creatinine (r=-0.956, p<0.001) and significant positive correlation with eGFR (r=0.914, p<0.001) (Figure 3).

Figure 3: Correlations of ADC with laboratory parameters.



The Logistic Regression Analysis for Establishing ADC as Predictor of DM showed that DM will be predicted ifD = 507.30 – 229.55ADC > 0Or ADC < 2.210. Considering stage 1 as the reference category, the Multinomial Logistic Regression Analysis for Establishing ADC as Predictor of DM Stages the following equation can be used to predict stages of DM, S2 = 673.0 – 312.3ADC > 0 for stage 2, S3 = 1674.4 – 797.3ADC > 0 for stage 3, S4 = 2118.0 – 1032.4ADC > 0 for stage 4 and S5 = 4065.7 – 2190.1ADC > 0 for stage 5If all the above equations gives negative results then either stage 1 or stage 0 (no DM) can be predicted (Table 3).

Table 3: Multinomial logistic regression analysis for establishing ADC as predictor of DM stages

Dependent	Independent	B	Std. Error	Sig.	% Accuracy
Stage 2	Intercept	673.0	148890.6	0.996	92%
	ADC	-312.3	69225.6	0.996	
Stage 3	Intercept	1674.4	230006.7	0.994	
	ADC	-797.3	109957.7	0.994	
Stage 4	Intercept	2118.0	248724.8	0.993	
	ADC	-1032.4	120745.8	0.993	
Stage 5	Intercept	4065.7	281601.9	0.988	
	ADC	-2190.1	144013.6	0.988	

DISCUSSION

Diabetes mellitus is a common disease in India with high prevalence of diabetic nephropathy especially among type 2 DM (9). The magnetic resonance imaging (MRI) techniques like diffusion-weighted imaging (DWI), blood oxygen level-dependent (BOLD) imaging, and contrast-enhanced MRI renography have a powerful ability in assessment of kidney functions.Regarding stages of diabetic nephropathy, our study found nephropathy stages as I (3.8%), stage II (3.8%), stage III (46.2%), stage IV (23.1%) and stage V (23.1%).

The mean GFR of study participants was significantly lower among patients with diabetic nephropathy ($p<0.001$). This finding is consistent with results of Rigalleau et al., (10) study in France which confirmed low mean GFR among patients with diabetic nephropathy that is used also in staging of nephropathy.Elevated hypertension and high proteinuria level are the main risk factors which increases severity of diabetic nephropathy.

Our study revealed that diabetic patients had mean MRI-ADC value for right kidney 1.86±0.22 x10-3 mm2/s and mean MRI-ADC of left kidney 1.85±0.2 x10-3 mm2/s, while the mean average MRI-ADC value for both kidneys was 1.86±0.2 x10-3 mm2/s. These findings are similar to ADC values reported by Goyal et al., (11) which documented lower MRI-ADC values for diabetic patients due to renal complications of diabetes. MRI-ADC means of study participants were significantly reduced among patients with diabetic nephropathy ($p<0.001$). This finding is in agreement with many previously reported studies like Inoue et al., (6) study in Japan and Ries et al., (5) study in France which reported significantly lower MRI-ADC values in patients with diabetic nephropathy in comparison to diabetic patients with no nephropathy and healthy population. Impaired kidney function could be acquired through abnormalities of chronic tubulointerstitial functions that lowers the renal water level and limited the fibrosis mediated diffusion of water molecules.

The MRI-ADC values are the reflection of different degrees of chronic tubule interstitial abnormalities attributed to declined renal oxygenation provokes nephropathy changesLow density of peritubular capillaries in diabetic nephropathy and non-diabetic nephropathy is due also to tubulointerstitial abnormalities that lead to parenchymal hypoxia. Lu et al., (7) study in USA suggested that medullary apparent diffusion coefficient and fractional anisotropy,

quantified by kidney diffusion tensor imaging, may be potential imaging biomarkers for diabetic nephropathy.

In present study, there was a significant decline in mean MRI-ADC value among patients with advanced stages of diabetic nephropathy ($p<0.001$). This finding coincides with results of Çakmak et al., (12) study in Turkey which found that MRI ADC values were prominently decreased along with advanced stages of diabetic nephropathy. Toya et al., (13) reported that MRI-ADC value was decreased with decrease of GFR but they did not reveal a significant correlation between ADC and GFR. However, many authors had shown that MRI-ADC values of kidney were decreased in different forms of acute and chronic renal diseases with a significant relationship between MRI-ADC and GFR values.

In another Japanese study, the mean MRI-ADC for kidney cortex and the medulla of patients with chronic or acute kidney failure were effectively decreased than population with normal function kidneys. Yalçin-Şafak et a., (14) study revealed a highly significant decline in MRI-ADC values at stage V diabetic nephropathy in comparison to healthy individuals. As the MRI-ADC value is related directly to water molecular and capillary perfusion in tissues, Changes in MRI-ADC value inform Radiologists on micro structural changes in kidneys. Water level changes in kidney tissues in addition to kidney blood and tubular flow lead to changes in ADC values.

CONCLUSION

The magnetic resonance imaging- Apparent diffusion Coefficient (ADC) value is an appropriate method for assessment and evaluation of diabetic nephropathy. Renal ADC values show a significant correlation with clinical stages of diabetic nephropathy, it is a reliable diagnostic tool for differentiation between diabetic nephropathy patients from diabetic patients without nephropathy. As a relatively simple and non-invasive tool without contrast media administration, renal quantitative DWI may potentially play a role in making clinical decisions in the follow-up of diabetic patients.

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