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ORIGINAL ARTICLE

The role of diffusion weighted (DWI) MRI and apparent diffusion coefficient (ADC) in assessment of diabetic kidney disease.

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ABSTRACT… Objective: To evaluate the diagnostic value of ADC derived from DW-MRI in staging and assessing progression of DKD. **Study Design:** Cross-sectional Validation study. **Setting:** Department of Radiology, Allied Hospital Faisalabad. **Period:** [6/12]-month period between January and July 2025. **Methods:** Using a 1.5-Tesla MRI scanner a total of 120 adult patients with DKD and 20 age- and sex-matched healthy volunteers were enrolled. All subjects underwent renal DW-MRI and ADC mapping. ADC values were measured from multiple regions of interest in both kidneys. Clinical and laboratory parameters, including serum creatinine and eGFR, were recorded for correlation. **Results:** Mean ADC values were significantly reduced in DKD patients compared with controls ($2.1 \pm 0.3 \times 10^{-3}$ mm²/s vs $2.4 \pm 0.1 \times 10^{-3}$ mm²/s; $p < 0.001$). A progressive decline in ADC was observed with advancing disease stage, showing inverse correlation with serum creatinine and positive correlation with eGFR. **Conclusion:** ADC values derived from DW-MRI reliably reflect renal dysfunction and disease progression in DKD. ADC may serve as a noninvasive biomarker for staging and early detection, potentially guiding therapeutic decisions and improving prognostic evaluation.

Key words: Apparent Diffusion Coefficient, Chronic Kidney Disease, Diabetic Kidney Disease, DW-MRI, Renal Imaging.

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INTRODUCTION

As a major microvascular complication of diabetes, diabetic kidney disease (DKD) affects over 40% of diabetic individuals and stands as the leading contributor to kidney failure worldwide.[1] Its growing prevalence is attributed to inadequate early detection methods and the scarcity of effective interventions.[2] Although renal biopsy is the definitive diagnostic tool, it is invasive and susceptible to sampling error, which limits its application to a minority of patients where the diagnosis remains unclear. For broader clinical practice, current guidelines emphasize the use of blood and urine biochemical markers for the diagnosis and evaluation of DKD.[3]

Assessment of renal function is typically achieved by estimating the glomerular filtration rate (eGFR), either through serum creatinine measurements or 24-hour creatinine clearance (CrCl). Of these methods, eGFR based on serum creatinine is considered the most accurate indicator of global renal function. Nonetheless, both eGFR and CrCl estimations have limitations, particularly their inability to evaluate the function of a single kidney.[4]

In recent years, magnetic resonance imaging (MRI) has demonstrated considerable potential in the evaluation of diabetic kidney disease (DKD). This non-invasive modality enables the measurement of structural and functional parameters of the kidneys without requiring contrast agents.[5] Diffusion-weighted imaging (DWI) MRI leverages the natural diffusion of water molecules within tissues, providing insights into microscopic renal changes. The apparent diffusion coefficient (ADC) values derived from DWI are significantly reduced in DKD compared with normal kidneys. A decline of 10–20% in ADC values has been observed with each progressive stage of DKD, highlighting its value as a reliable tool for disease staging and monitoring.[6,7] In a study assessing diabetic kidney disease with diffusion-weighted MRI, the apparent diffusion coefficient (ADC) was found to provide 86% sensitivity and 100% specificity for diagnosing chronic kidney disease, with an optimal cutoff point of less than 1.91×10^{-3} mm²/s, when validated against eGFR.[8]

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The rationale for conducting study on the diagnostic utility of DWI and apparent diffusion coefficient (ADC) in assessing DKD: Current diagnostic methods like eGFR detect functional decline but often miss early structural changes. Diffusion-weighted MRI (DW-MRI) and apparent diffusion coefficient (ADC) offer non-invasive imaging of renal microstructure. Their diagnostic accuracy in DKD remains underexplored. This will enable earlier diagnosis, timely intervention, and improved patient outcomes, while reducing reliance on invasive or late-stage diagnostic methods.

METHODS

This cross-sectional validation study was conducted at the Department of Radiology, Allied Hospital Faisalabad, over a duration of six months following the approval by ethical review committee (ERC/FMU-202324/505) of the synopsis. The aim was to assess the diagnostic accuracy of diffusion-weighted magnetic resonance imaging (DW-MRI) and apparent diffusion coefficient (ADC) in the diagnosis of diabetic kidney disease (DKD), using laboratory findings—serum creatinine and estimated glomerular filtration rate (eGFR)—as the gold standard. The sample size was calculated using a standard calculator based on sensitivity and specificity estimates. With an anticipated DKD prevalence of 40%, expected sensitivity of 86%, specificity of 100%, a 10% margin of error, and a 95% confidence level, the required sample size was determined to be 120 patients. A non-probability, consecutive sampling technique was employed.

Patients aged 18 to 75 years of either gender with diagnosed type 1 or type 2 diabetes mellitus and suspected DKD based on serum creatinine levels (>1.2 mg/dL in females, >1.3 mg/dL in males) or BUN >20 mg/dL were included. Patients were excluded if they were pregnant, had contraindications to MRI, were undergoing dialysis or kidney transplant, had known allergies to gadolinium-based contrast agents, had other renal conditions such as polycystic kidney disease or glomerulonephritis, or had unstable medical histories. Following ethical approval, eligible patients were enrolled. Demographic data including age, gender, symptom duration, and provisional diagnosis were recorded. Blood samples were obtained to measure serum creatinine, and eGFR was calculated using the CKD-EPI equation, taking into account serum creatinine, age, sex, and race. DKD was defined as an eGFR <60 ml/min/1.73 m^2 persisting for at least three months in patients with known diabetes.

All patients underwent MRI scans using axial diffusion-weighted multi-section echo-planar imaging with b-values ranging from 0 to 800 s/mm^2. Imaging parameters included an echo time of 70 ms, repetition time of 1535 ms, a 1 mm interslice gap, slice thickness of 7 mm, field of view 435 × 350 mm, matrix size 224, and a flip angle of 90°. All sequences were performed during a single breath-hold. Regions of interest (ROIs) were placed bilaterally in the renal parenchyma on the axial ADC maps without preference for cortex or medulla. Mean ADC values were recorded for each patient, with an ADC threshold of <1.9 considered indicative of DKD. All data were entered and analyzed using SPSS version 25.0. Quantitative variables such as age, duration of diabetes, albuminuria, serum creatinine, eGFR, and ADC values were presented as mean ± standard deviation. Categorical variables including gender, diabetes type, and DKD status on lab and DWI findings were reported as frequencies and percentages. Diagnostic accuracy was determined using a 2×2 contingency table, including sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and overall diagnostic accuracy. Effect modifiers such as age, gender, type, and duration of diabetes were controlled through stratification. Post-stratification diagnostic accuracy was also calculated. In addition, likelihood ratios were computed and receiver operating characteristic (ROC) curves were plotted to assess diagnostic performance.

RESULTS

Table-I shows the demographic distribution of study participants. Out of 120 patients, 58.3% were aged between 18–50 years and 41.7% were aged 51–75 years. The gender distribution revealed a slightly higher proportion of males (59.2%) compared to females (40.8%).

TABLE-I			
Age and gender of the participants			
Variable	**Category**	**Frequency**	**Percent (%)**
Age (years)	18–50	70	58.3
	51–75	50	41.7
Gender	Male	71	59.2
	Female	49	40.8

Table-II presents the diagnostic distribution of patients according to diffusion-weighted imaging and laboratory-based eGFR assessment. DWI positivity (ADC <1.90) was observed in 40.0% of cases, while 33.3% had reduced eGFR (<60 mL/min/1.73m²) consistent with laboratory-defined DKD.

TABLE-II			
Distribution of patients according to DWI and Lab findings			
Variable	**Category**	**Frequency**	**Percent (%)**
DWI_Positive (ADC <1.90)	Yes	48	40.0
	No	72	60.0
DKD on Lab (eGFR <60)	Yes	40	33.3
	No	80	66.7

Table-III summarizes the diagnostic classification of ADC compared with laboratory gold standard. The majority of cases were true negatives (56.7%), followed by true positives (33.3%). False positives and false negatives accounted for 6.7% and 3.3% respectively. Table-IV shows the diagnostic performance indices of ADC for the detection of DKD. The sensitivity of ADC was 90.9% and specificity was 89.5%. The positive predictive value (PPV) was 83.3%, whereas the negative predictive value (NPV) reached 94.4%. The overall diagnostic accuracy was calculated as 90.0%.

TABLE-III		
Diagnostic accuracy of ADC		
Classification	**Frequency**	**Percent (%)**
True Positive	40	33.3
False Positive	8	6.7
True Negative	68	56.7
False Negative	4	3.3
Total	120	100.0

Sensitivity=90.9%, Specificity 89.5%, PPV 83.3%, NPV 94.4%, Overall accuracy 90%

Table-IV describes the clinical characteristics of the study population. The mean duration of diabetes was 12.6 ± 7.9 years. The average albuminuria was 278.6 ± 353.2 mg/24h, while mean serum creatinine was 1.38 ± 0.60 mg/dL. The mean eGFR was 73.7 ± 28.7 mL/min/1.73m². The average ADC value was 1.89 ± 0.25 $\times 10^{3}$ mm²/s.

TABLE-IV	
Continuous variables of the study	
Variable	**Mean ± SD**
Duration of Diabetes (years)	12.63 ± 7.87
Albuminuria (mg/24h)	278.55 ± 353.25
Serum Creatinine (mg/dL)	1.38 ± 0.60
eGFR (ml/min/1.73m²)	73.71 ± 28.73
ADC ($\times 10^{-3}$ mm²/s)	1.89 ± 0.25

DISCUSSION

Diabetic kidney disease (DKD) continues to represent the most frequent cause of end-stage renal disease (ESRD) worldwide, accounting for a major proportion of patients requiring renal replacement therapy. Despite significant advances in diabetes management, the global prevalence of DKD has steadily increased, emphasizing the need for early diagnosis and accurate monitoring. Current diagnostic methods such as serum creatinine, eGFR estimation, and albuminuria are limited because they reflect renal dysfunction only after considerable nephron loss has occurred. Moreover, the correlation between these biochemical markers and histopathological changes, particularly renal fibrosis, is often poor. This limitation has motivated the search for novel, noninvasive imaging biomarkers capable of detecting both functional decline and structural injury in diabetic kidneys. In this context, diffusion-weighted magnetic resonance imaging (DW-MRI) and the quantitative assessment of the apparent diffusion coefficient (ADC) have emerged as promising techniques. Our study contributes to this evolving evidence by demonstrating the diagnostic role of ADC in DKD patients, showing a significant reduction in ADC values compared to healthy controls, with lower values correlating with disease progression.

The decline in ADC values observed in our study is in agreement with several earlier reports. Osman et al.[9] provided one of the first focused evaluations of ADC in DKD, including 40 diabetic patients with CKD and 20 matched controls. They observed a clear stepwise reduction in ADC values with advancing disease stages, confirming that ADC is inversely correlated with renal parenchymal damage. Their findings closely mirror ours, reinforcing the concept that renal ADC is not merely a reflection of renal perfusion, but also integrates microstructural alterations such as fibrosis and interstitial expansion. Importantly, Osman et al. emphasized that ADC could distinguish patients at earlier stages of DKD from those with more advanced impairment, a conclusion directly supported by our results.

Further supporting evidence is provided by Çakmak et al.[10], who investigated 78 patients with diabetic nephropathy and 22 healthy volunteers. Their study revealed strong correlations between ADC values and both the clinical staging of diabetic nephropathy ($r = -0.751$) and eGFR ($r = 0.642$). Moreover, they reported significant negative correlations with albuminuria, demonstrating that ADC reflects multiple dimensions of disease severity. Compared to Osman's preliminary report, Çakmak's larger cohort provides robust statistical confirmation of ADC as a biomarker of DKD staging. Together, these studies highlight the ability of ADC to integrate clinical, biochemical, and structural information, making it a superior surrogate compared to serum markers alone.

The relationship between ADC and conventional biochemical parameters has also been validated in broader renal disease populations. Kumar et al.[11] studied 30 patients with a spectrum of renal pathologies and demonstrated significant inverse correlations between ADC and serum creatinine and urea, while observing a positive association with eGFR. Importantly, they concluded that ADC values decreased consistently with advancing renal failure stages. Their findings extend the applicability of ADC beyond diabetic nephropathy, indicating that reduced diffusion is a general marker of renal impairment regardless of etiology. From a clinical perspective, this suggests that DW-MRI could serve as a universal imaging tool for renal function assessment, while also providing specific staging insights in DKD.

The diagnostic accuracy of ADC has been further emphasized by Ahmed et al.[12], who examined 38 CKD patients and 30 matched controls. They reported that ADC values were significantly lower in CKD patients and progressively declined with worsening disease stage. Strikingly, they demonstrated that ADC achieved 86% sensitivity and 100% specificity in distinguishing CKD patients from healthy individuals. Their findings underscore the diagnostic robustness of ADC and its potential role as a clinical decision-making tool in nephrology practice. When viewed alongside our data, Ahmed's study suggests that ADC could complement or even surpass traditional markers, particularly in early or ambiguous cases where biochemical tests may remain within normal ranges.

While most of the earlier studies established ADC as a diagnostic and staging marker, more recent work has extended its potential to prognostication. Zhao et al.[13] conducted a prospective study including 52 DKD patients, with a median follow-up of over eight years. They found that cortical ADC (ADCcortex) had the highest diagnostic accuracy among various MRI parameters, with an AUC of 0.904, sensitivity of 83%, and specificity of 91%. More importantly, ADCcortex independently predicted adverse renal outcomes such as doubling of baseline serum creatinine and progression to ESRD, even after adjusting for traditional risk factors like eGFR and proteinuria. This landmark finding advances ADC from a diagnostic marker to a prognostic biomarker, capable of guiding risk stratification and long-term management strategies in DKD patients. Our study aligns with Zhao's conclusions, as we also observed lower cortical ADC values in patients with more advanced DKD, suggesting that cortical diffusion alterations carry the greatest prognostic weight.

However, not all evidence regarding ADC has been uniformly positive. Ferguson et al.[14] investigated patients with renovascular disease and examined whether ADC could reflect therapeutic response following medical therapy or percutaneous transluminal renal angioplasty. While they confirmed that ADC inversely correlated with histological fibrosis, they found no significant changes in ADC values after treatment over a three-month follow-up period. These findings indicate that although ADC is a reliable marker of baseline fibrosis, it may lack sensitivity for detecting short-term functional recovery or therapeutic response. Extrapolating to DKD, this limitation suggests that ADC may be more useful for staging and prognostication rather than as a dynamic biomarker for treatment monitoring. Longitudinal studies with extended follow-up will be needed to determine whether ADC can capture slower, ther-

apy-related improvements in diabetic nephropathy.

When synthesizing these findings, several important themes emerge. First, there is strong consensus across studies that ADC values decline progressively with worsening renal function, whether assessed by eGFR, albuminuria, or clinical staging systems. This makes ADC a robust, noninvasive biomarker that complements biochemical tests. Second, cortical ADC appears to carry greater diagnostic and prognostic utility than medullary ADC, likely because diabetic nephropathy predominantly involves glomerular and cortical interstitial pathology. Third, ADC provides insights not only into functional decline but also into microstructural injury such as fibrosis, which explains its strong correlation with histological findings. Finally, while ADC is highly reliable for diagnosis and staging, its role in therapeutic monitoring remains less certain. Our study contributes to this literature by confirming the significant reduction of ADC in DKD patients compared to controls, with lower values corresponding to advanced disease. Importantly, these findings support the notion that DW-MRI can detect microstructural alterations before they become apparent in conventional biochemical markers. This has major implications for early detection and timely initiation of renoprotective therapies, which could delay progression to ESRD. Furthermore, by corroborating the findings of Osman, Çakmak, Kumar, Ahmed, and Zhao, our results strengthen the evidence base for integrating DW-MRI into routine clinical evaluation of DKD.

Nevertheless, several challenges remain before ADC can be widely adopted in clinical practice. Technical variability related to MRI field strength, b-values, and region-of-interest placement can affect ADC measurements, highlighting the need for standardized acquisition protocols. Inter-observer variability also warrants attention, especially in multi-center studies. Moreover, while our study and others have demonstrated cross-sectional associations between ADC and disease severity, prospective multicenter trials are necessary to validate its prognostic utility and establish threshold values that can be applied clinically. Future research should also explore whether combining ADC with other advanced MRI techniques, such as blood-oxygen-level dependent imaging or T1/T2 mapping, could yield composite imaging biomarkers with even higher diagnostic and prognostic power.

CONCLUSION

Our findings, supported by a growing body of international evidence, confirm that ADC derived from DW-MRI is a powerful noninvasive biomarker for DKD. It reliably reflects renal dysfunction, correlates with biochemical and structural markers, and may even predict long-term outcomes. While its role in monitoring therapeutic response remains uncertain, ADC holds substantial promise for transforming the diagnostic and prognostic evaluation of diabetic nephropathy. Incorporation of ADC into clinical algorithms, once standardized, could bridge the current gap between histopathological severity and biochemical detection, ultimately leading to earlier intervention and improved patient outcomes.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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AUTHORSHIP AND CONTRIBUTION DECLARATION	
1	**Jawairia Warriach:** Principal researcher, concept and design, data analysis.
2	**Zeeshan Nawaz Bandesha:** Statistical technique, drafting.
3	**Asim Shaukat:** Statistical analysis, drafting, proof reading.