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Early Detection of Diabetic Nephropathy: The Added Value of Functional MRI

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ABSTRACT

Background: Diffusion Tensor Imaging (DTI) and renal tractography provide valuable insights into the microstructural organization of the kidney and enable the detection of alterations in diffusion parameters by quantifying fractional anisotropy (FA) and apparent diffusion coefficient (ADC).

Objectives: This study aimed to evaluate whether advanced functional MRI techniques specifically, quantitative DTI metrics and renal fiber tractography can assist in the early detection of diabetic nephropathy.

Patients and methods: Sixty patients with type 2 diabetes mellitus (DM) were enrolled in the study and categorized into two groups based on the presence of normoalbuminuria or microalbuminuria. In addition, a control group consisting of 20 age-matched healthy individuals without a history of diabetes was included for comparison. All participants, including patients and controls, underwent MRI scanning using a 1.5 Tesla GE Signa system.

Results: Patients with microalbuminuria showed significantly lower cortical and medullary FA values and higher cortical ADC values. Tractography revealed reduced fiber count and disorganized tracts in this group. Cortical FA correlated positively with estimated glomerular filtration rate. (eGFR) and negatively with albuminuria, while ADC showed the opposite. Cortical FA demonstrated the highest diagnostic accuracy (AUC = 0.88) for detecting early renal microstructural changes.

Conclusions: DTI and renal tractography effectively detect early renal microstructural changes in diabetic nephropathy. Cortical FA is a sensitive biomarker for early dysfunction, showing strong diagnostic performance and correlation with renal function and albuminuria.

Keywords: Diabetic nephropathy, Diffusion Tensor Imaging, FA, ADC.

INTRODUCTION

Diabetic nephropathy (DN) is the leading cause of end-stage renal disease (ESRD). Its global prevalence is steadily increasing and is expected to rise further in parallel with the growing incidence of T2DM [(1)]. Health care policies must be modified to comprehensive care for individuals with chronic kidney disease (CKD) and that resources are used effectively for early diagnose ESRD [(1)].

Discovering biomarkers for early stages of DN patients, will allow patients of high-risk groups to receive focused, intensive treatment, and support clinical trials for new therapeutic options. Despite the presence of several risk factors linked to progression of DN, their predictive value in assessment of disease progression in diabetic patients remains limited [(2)].

The diagnosis and prognosis of the patients with renal failure, as well as follow up of the disease progression, depends mainly on different laboratory parameters including serum creatinine and the estimated glomerular filtration rate (eGFR).However, these parameters have low sensitivity and also are not specific for grading as they tend to change only in the advanced stages of renal damage [(3)]. It is evident that magnetic resonance imaging (MRI) techniques have been significantly changing over the past decades, primarily due to technological advancements. Among the many sophisticated MRI instruments is functional magnetic resonance imaging (FMRI) [(3)].

FMRI has demonstrated significant promise in evaluating the pathology of kidney in diabetic renal diseases. It is a noninvasive method of obtaining additional kidney structural as well as functional biomarkers, all without requiring the use of contrast agents [(4)]. Currently, the primary fMRI techniques used for integrated evaluation of morphology and function of the kidneys affected by diabetes include diffusion-weighted imaging (DWI-MRI) and diffusion tensor imaging (DTI) [(5)]. DTI is a novel MRI technique that estimates random movement of water while assessing global molecular diffusion by determining the preferred direction of diffusion by measuring fractional anisotropy (FA) and the apparent diffusion coefficient (ADC) [(6)].

Since DTI and renal tractography can evaluate organized renal structure and identify the decrease in diffusion parameters, which may be brought on by tubular atrophy, fibrosis in the interstitial space, accumulation of inflammatory cells, and glomerular fibrosis, they have been tested for monitoring renal tissue injury in patients affected by diabetic kidney disease (DKD) [(7)]. Utilizing functional MRI (fMRI) to assess structural and functional alterations in the renal tissue in patients with DKD remains limited and is not yet widely adopted in clinical settings [(7)].

The aim of our study was to investigate the contribution of quantitative DTI parameters and fiber tractography in the early detection of diabetic nephropathy. DTI metrics such as FA and ADC were compared between healthy subjects and patients with early diabetic nephropathy who were clinically defined by the presence of normo-albuminuria or micro-albuminuria.

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PATIENTS AND METHODS

This prospective case-control study included a total of 60 patients diagnosed with type 2 diabetes mellitus (DM) and 20 age and sex matched healthy controls without a history of diabetes who were included for comparison. Participants were recruited through referrals from the Internal Medicine Department to the Radio-diagnosis Department, Tanta University Hospital, during the period from December 2023 to April 2025.

The included subjects were divided into two groups: **Group 1** (normo-albuminuric) consisted of 30 patients with a urinary albumin-to-creatinine ratio (UACR) <30 mg/g, and **Group 2** (micro-albuminuric) consisted of 30 patients with a UACR between 30–300 mg/g. In addition, a **control group** of 20 age and sex-matched healthy individuals was included. These individuals had no history of diabetes and showed normal laboratory parameters, including serum creatinine, urinary protein, fasting plasma glucose, and glycated hemoglobin (HbA1c).

Type 2 diabetic patients aged 18 to 65 years, diagnosed according to the 2007 American Diabetes Association (ADA) criteria were included in the study. Eligible participants had no coexisting disorders influencing kidney function (such as gout, nephrotic syndrome or blood disorders); were not taking medications known to affect renal perfusion and had no known contraindications of the MRI examination.

Exclusion criteria: Patients with pyelonephritis, urinary tract infection, small-sized kidneys, loss of cortico-medullary differentiation, or abnormal renal anatomy on MRI were excluded. Additional exclusion criteria included medically unstable individuals, those with claustrophobia, and patients with cardiac pacemakers or other MRI-incompatible implants. Healthy controls were excluded if they had any abnormal laboratory results.

All participants underwent a comprehensive medical history assessment included sex, age, body mass index (BMI), duration of diabetes and diabetic medications, family history and risk factors of renal diseases, present history of current illness, onset, course, duration and laboratory investigations including serum creatinine with estimated glomerular filtration rate (eGFR), albumin-to-creatinine (A/C) ratio, urine analysis, and (glycated hemoglobin) HbA1c.

MRI imaging acquisition:

A 1.5 GE Signa 1.5T MRI system was used to scan all patients and control volunteers at Tanta University Radiodiagnosis Department MRI unit, using a standard 16-channel body coil. All metal pins were removed by the patients before the scan.

The standard MRI protocol for kidney studies incorporated a series of sequences including 2D coronal FIESTA with respiratory triggering, axial SSFSE T2-weighted with respiratory gating, axial breath-hold FSPGR, and T1-weighted dual-phase imaging (in and out of phase).

- **Diffusion tensor imaging:** A high-resolution 3D T1-weighted spoiled gradient echo (SPGR) pulse sequence with the following parameters was acquired : repetition time (TR)=9.7ms, echo time (TE)=4.6ms, inversion time (TI)=400ms, flip angle=35°, 124 slices with a slice thickness of 0.8mm, matrix size of 208×170, and a field of view (FOV) of 23cm.
- DTI was performed using a single-shot spin echo-planar imaging sequence with 40 diffusion directions. Imaging parameters included TR=8,830ms, TE=80ms, a 112×110 matrix, and 2mm isotropic voxels. The field of view was 224×224×120mm, with a b-value of 800s/mm². A total of 60 slices were acquired with a reconstructed voxel size of 1.75mm.
- **Data post-processing:** All the conventional MRI and DTI data were exported to an off-line workstation (Advantage 4.7, GE Medical Systems) for analysis. All MRI scans underwent visual inspection to identify artifacts that could potentially compromise data analysis or interpretation. Prior to DTI analysis, morphological evaluation was performed in consensus by two radiologists. For each participant, renal dimensions (including longitudinal length and thickness of parenchymal) as well as cortico-medullary differentiation (CMD) were assessed using T1-weighted images.
- DTI analysis was performed for all participants for each kidney. The DTI data were reconstructed into color-coded directional maps and DTI maps reflecting key diffusion metrics including FA and ADC maps.
- Circular regions of interests (ROIs) with a mean pixel size of 50 mm², were placed on each map: "In each kidney, three cortical ROIs and three medullary ROIs were positioned in the superior, mid, and inferior poles", with care taken to avoid the renal vasculature and collecting structures.
- Mean ADC and FA values were derived from DTI maps for each ROI. Tractography was initiated from these seed points and qualitatively evaluated in both cortical and medullary regions for alignment and coherence of diffusion tracts.
- Data obtained for anatomical standard sequences, ADC map, FA map and tractography data including tracts counts and length were measured then compared in both patients and control groups and correlated with laboratory data of the patients.
- To ensure privacy, a unique code was allocated to every participant, and data were anonymized in accordance with ethical guidelines.

Ethical approval:

This study was approved by the Research Ethics Committee of the Faculty of Medicine, Tanta University. Written informed consent was obtained

from all participants after a clear explanation of the study's purpose. Each participant was assigned a confidential code number to ensure anonymity. The study protocol adhered to the Declaration of Helsinki, the ethical standard of the World Medical Association for research involving human subjects.

Statistical analysis

Data were analyzed using SPSS version 26.0. Normality was evaluated with the Shapiro-Wilk test and histograms. Quantitative variables were expressed as mean ± SD and compared using unpaired t-tests, while categorical data were analyzed using Chi-square or Fisher's exact test. ROC curve analysis assessed diagnostic accuracy, with AUC>50% considered acceptable. A p-value below 0.05 was deemed statistically significant.

RESULTS

60 patients with type 2 diabetes mellitus and twenty age- and sex-matched healthy individuals served as a control group were recruited. Regarding grouping, we divided patients into two groups: 30 patients with normal albuminuria (albuminuria <30 mg/g), 30 patients with micro-albuminuria (albuminuria 30-300 mg/g). Demographic and laboratory characteristics, including the age, sex distribution, clinical and laboratory findings across the three groups (Table 1**)**.

No significant differences were observed regarding age, sex distribution, or BMI among the normo-albuminuria, micro-albuminuria, and control groups (p>0.05). Hypertension was significantly more prevalent among diabetic patients, affecting 70% of those with normo-albuminuria and 90% with micro-albuminuria, compared to the control group (p<0.001).

The albumin-to-creatinine (A/C) ratio was markedly higher in the micro-albuminuria group compared to the normo-albuminuria group (p=0.002). Patients with micro-albuminuria had a significantly longer duration of diabetes and poorer glycemic control, as evidenced by higher HbA1c levels, compared to those in the normo-albuminuric group (p<0.05). eGFR decline aligned with disease progression, consistent with diabetic nephropathy staging (Table 1).

Table (1): Demographic and clinical data of the studied groups

Variable	Group 1: Normo-albuminuria (n=30)	Group 2: Micro-albuminuria (n=30)	Control Group (n=20)	p-value
Age (years)	64.5 ± 6.2	57.8 ± 8.1	63.2 ± 10.3	0.15 (KW)
Sex (% female)	6 (60%)	6 (60%)	6 (60%)	1.00 (χ^2)
Hypertension (% yes)	7 (70%)	9 (90%)	0 (0%)	**<0.001 (FET)**
BMI (kg/m²)	28.2 ± 2.5	27.6 ± 3.8	29.1 ± 3.2	0.41 (ANOVA)
Diabetes Duration (years)	10 [5–12]	12.5 [7–20]	N/A	0.10 (MWU)
eGFR (mL/min/1.73 m²)	58.2 [45–70]	55.1 [40–65]	N/A	0.32 (MWU)
A/C Ratio	8.7 [5.1–14.9]	71 [36.8–129]	N/A	0.002 (MWU)
HbA1c (%)	9.4 ± 1.8	8.9 ± 1.6	N/A	0.45 (MWU)

BMI= Body mass index; eGFR= Estimated Glomerular Filtration Rate; A/C Ratio= Albumin-to-Creatinine Ratio; HbA1c= Hemoglobin A1c; KW= Kruskal-Wallis test; MWU= Mann-Whitney U test; FET= Fisher's Exact Test; χ^2= Chi-square test; Significant p-values (p < 0.05) are shown in **bold.**

The average FA values of the ROIs in the studied patients showed that, as regard renal cortex, the control group demonstrated notably higher FA values (0.39 ± 0.01) when compared to both the normo-albuminuria group (0.29 ± 0.05; p = 0.001) and the micro-albuminuria group (0.25 ± 0.04; p < 0.001). As

for renal medulla, patients with micro-albuminuria showed significantly lower FA values (0.41 ± 0.03) than those observed in the control group (0.48 ± 0.02; p = 0.02).

As regard ADC values of the studied groups, cortical ADC values were significantly elevated in patients with micro-albuminuria (1.78 ± 0.12 $\times 10^{-3}$ mm^2/s) compared to those with normal-abuminuria (1.63 ± 0.15 $\times 10^{-3}$ mm^2/s, p = 0.03), while medullary ADC values did not show any statistically significant differences between the groups (p = 0.12)**.**

Differences in diffusion properties among the control, normo-albuminuric, and micro-albuminuric groups, based on diffusion tractography data, revealed that the control group exhibited a uniform and organized tract arrangement extending outwardly in a radial pattern within the renal medulla.

The average fiber count and tract length in the control group were 32.0 ± 6.0 and 8.2 ± 1.3 mm, respectively. Similar findings were also observed in the normo-albuminuric group. On the other hand, the micro-albuminuric group demonstrated a marked reduction in both the number and length of diffusion tensor tracts when compared to the control and normo-albuminuric groups, with a mean tract count of 27.5 ± 3.5 and a tract length of 7.6 ± 0.7 mm (p < 0.05). Additionally, this group showed premature interruption and disorientation of the tracts **(Table 2).**

Table (2): DTI parameters across studied groups

DTI Parameter	Group 1: Normo-albuminuria	Group 2: Micro-albuminuria	Control Group	p-value	Post-hoc Comparisons
FA Cortex	0.29 ± 0.05	0.25 ± 0.04	0.39 ± 0.01	<0.001 (KW	**Group 1 vs. Control group: p=0.001 Group 2 vs. Control group: p<0.001**
FA Medulla	0.45 ± 0.03	0.41 ± 0.03	0.48 ± 0.02	**0.02 (KW)**	**Group 2 vs. Control group: p=0.02**
ADC Cortex ($\times 10^{-3}$ mm^2/s)	1.63 ± 0.15	1.78 ± 0.12	1.60 ± 0.10	**0.03 (KW)**	**Group 1 vs. Group 2: p=0.03**
ADC Medulla ($\times 10^{-3}$ mm^2/s)	1.51 ± 0.15	1.48 ± 0.12	1.65 ± 0.20	0.12 (KW)	–
Track counts	32.0 ± 6.0	32.6 ± 5.0	27.5 ± 3.5	**0.035**	
Track length (mm)	8.1 ± 1.3	8.2 ± 1.0	7.6 ± 0.7	**0.018**	

FA= Fractional Anisotropy; ADC= Apparent Diffusion Coefficient; KW= Kruskal-Wallis test.

Post-hoc comparisons performed using Dunn's test with Bonferroni correction; Significant p-values (<0.05) in **bold**.

Correlation analysis between DTI parameters and clinical variables across the three studied groups revealed that cortical FA was positively correlated with eGFR, indicating better renal function with higher FA values. Additionally, cortical FA was inversely correlated with the albumin-to-creatinine (A/C) ratio (ρ = -0.58, $p < 0.01$), suggesting that increased albuminuria was associated with reduced microstructural integrity.

Conversely, ADC values showed a significant negative correlation with eGFR (ρ = -0.55, $p < 0.01$), implying that higher ADC values were linked to impaired renal function. A significant positive correlation between cortical ADC and the A/C ratio was also found ($\rho = 0.61$, $p < 0.01$), indicating that increased diffusivity is associated with elevated albuminuria levels **(Table 3).**

Table (3): Correlation between DTI parameters and clinical variables

DTI Parameter	eGFR	A/C Ratio	HbA1c	Diabetes Duration
FA Cortex	0.62**	-0.58**	-0.32	-0.41*
FA Medulla	0.49*	-0.51*	-0.25	-0.38
ADC Cortex	-0.55**	0.61**	0.29	0.44*
ADC Medulla	-0.31	0.37	0.18	0.22

FA= Fractional Anisotropy; ADC= Apparent Diffusion Coefficient; eGFR= Estimated Glomerular Filtration Rate; A/C Ratio= Albumin-to-Creatinine Ratio; HbA1c= Hemoglobin A1c; **p<0.01; *p<0.05. Correlations calculated for diabetic groups (normo-albuminuria + micro-albuminuria, n=60).

The post-hoc analysis demonstrated significant differences in cortical FA among the studied groups, compared to control group both normo-albuminuria and micro-albuminuria groups exhibited significantly reduced cortical FA ($p < 0.001$ for both), with the latter showing further decline compared to normoalbuminuria ($p = 0.014$). A significant reduction in medullary FA was observed in micro-albuminuria group relative to healthy controls ($p = 0.012$), pointing to initial structural changes in renal medulla.

Cortical ADC values were markedly increased in the micro-albuminuria group compared to control group ($p = 0.026$), reflecting potential edema or inflammation, and it was insignificantly different between normo-albuminuria and micro-albuminuria groups ($p = 0.112$). The medullary region exhibited no statistically significant variation in ADC values across the three groups ($p > 0.05$), indicating preserved medullary diffusion properties in early diabetic nephropathy stages **(Table 4).**

Table (4): Pairwise Comparisons of DTI parameters across groups (Dunn's Post-Hoc Test)

Comparison	FA Cortex (p)	FA Medulla (p)	ADC Cortex (p)
Control group vs. normo-albuminuria group	**<0.001**	0.210	0.423
Control group vs. Micro-albuminuria group	**<0.001**	**0.012**	**0.026**
Normo-albuminuria group vs. Micro-albuminuria group	**0.014**	0.078	0.112

Assessment of the diagnostic performance of the measured DTI parameters demonstrated that, as regard FA, the highest area under the curve (AUC) was observed for the renal cortex (0.88, $p < 0.001$), where an FA value of ≤0.30 was able to detect early renal microstructural changes with 85% sensitivity and 82% specificity, while regarding the diagnostic performance of the measured ADC values, the cortical region showed an AUC of 0.76 ($p < 0.001$), where an ADC value of $\leq 1.70 \times 10^{-3}$ mm²/s yielded 78% sensitivity and 70% specificity, so it can support the diagnosis but is less reliable alone **(Figure 1).**

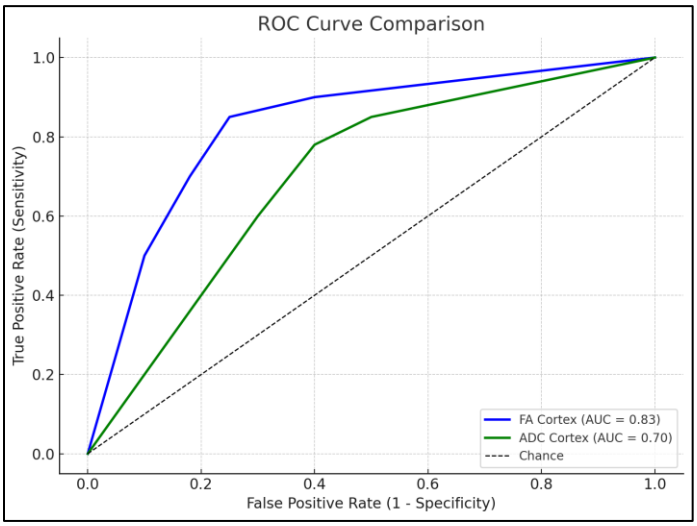

Figure (A): ROC curve analysis of the diagnostic performance of the measured DTI parameters.

CASE (1)

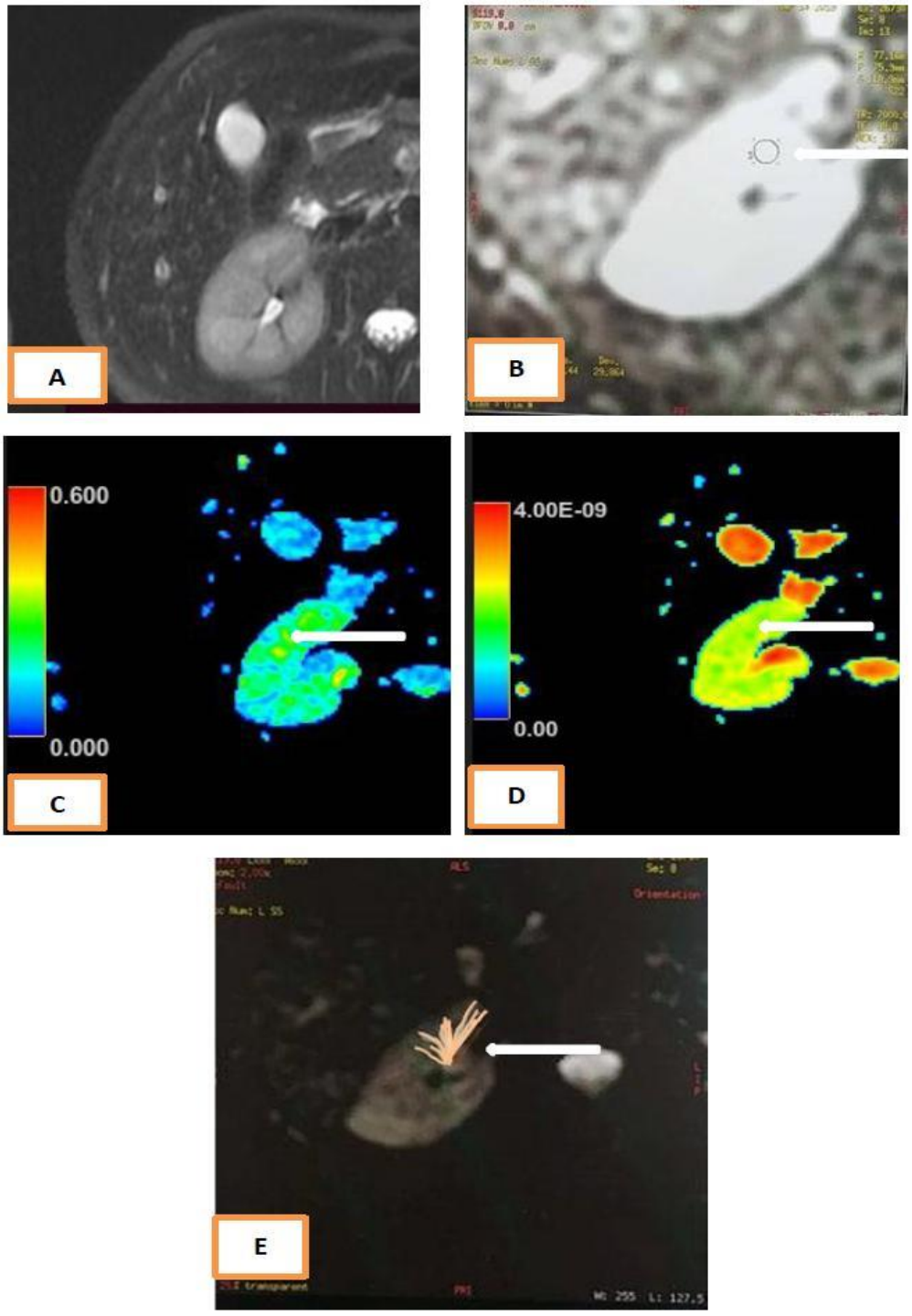

Figure (2): A 27-year-old male subject in the control group with an eGFR of 94 ml/min. Axial T2WI of the right kidney. **(A)** showing no significant abnormal findings. DTI b0 image **(B)** medullary ROI is defined in the mid-region of the right kidney (white arrow), with corresponding FA value at FA map **(C)** of 0.329, ADC value at ADC map **(D)** of 2×10^{-3} mm /s, Fiber tractography reconstruction from the identified ROI **(E**) reveals an average number of tracts, arranged regularly within the medulla and oriented radially (white arrow).

CASE (2)

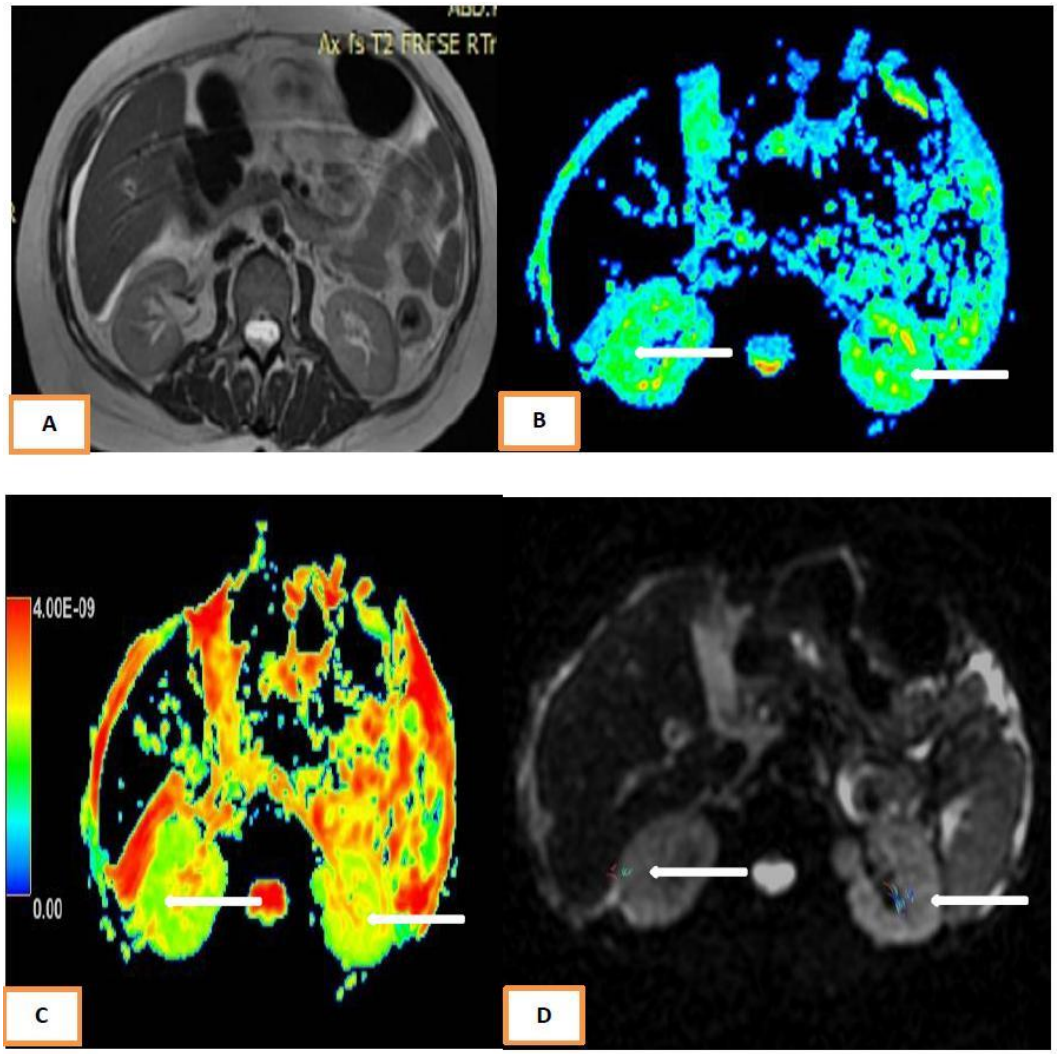

Figure (3): A 60-year-old woman with a medical history significant for T2DM and chronic hypertension, diagnosed clinically with bilateral diabetic nephropathy with an e-GFR of 40 ml/min/1.73 m2 & micro-albumineria. Axial T2WI **(A)** of both kidneys showing no significant abnormal findings. Axial FA map **(B)** showing focal areas of reduced medullary FA values (white arrows), axial ADC map **(C)** showing focal areas of increased medullary ADC values(white arrows). Fiber tractography reconstruction **(D)** reveals a decreased number of tracts in both kidneys, with no evident preferential alignment (white arrows).

CASE 3

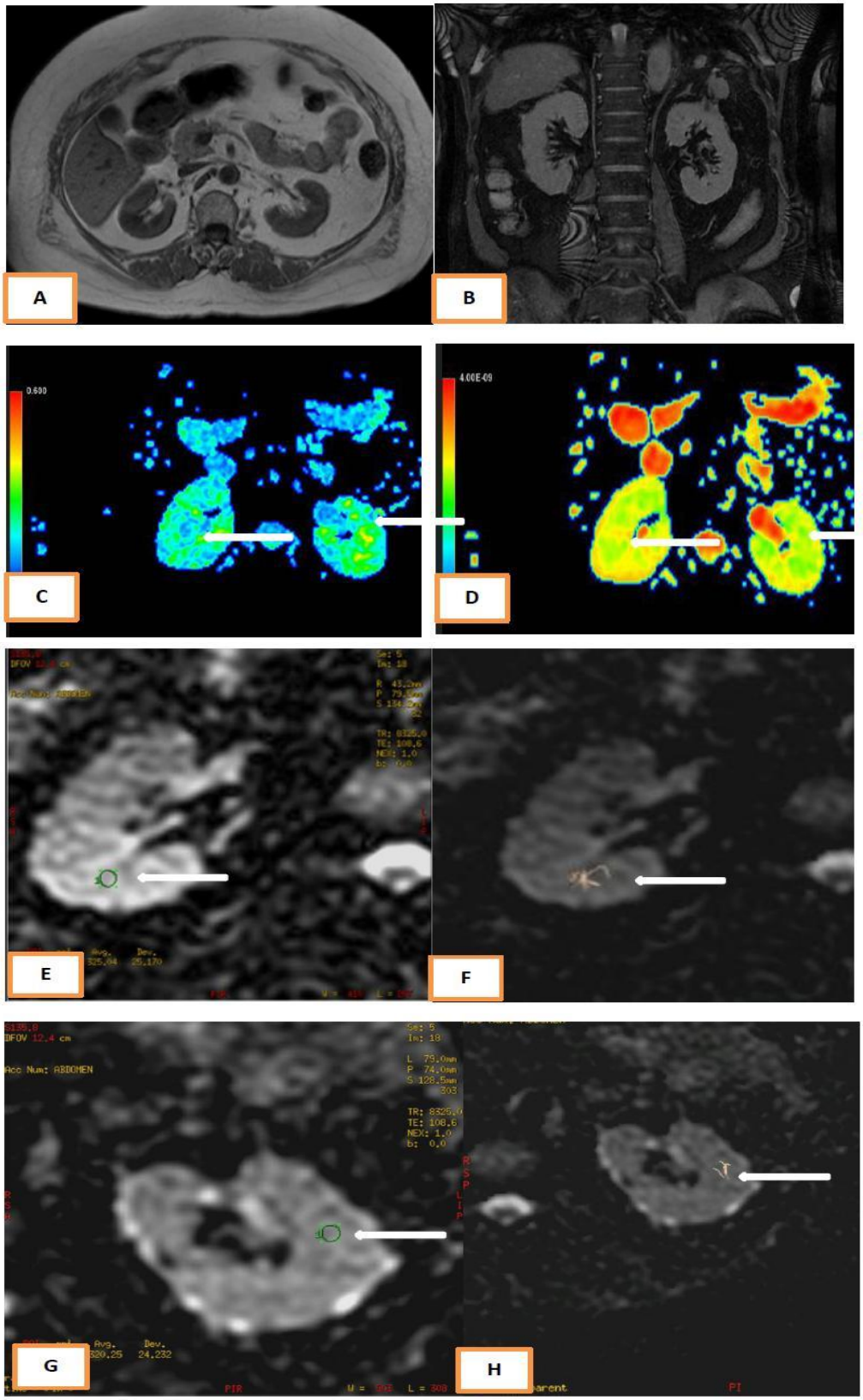

Figure (4): A 50-year-old male patient with a history of T2DM, diagnosed clinically with bilateral diabetic nephropathy with normal-albuminurea (albuminurea 28 mg/g) coronal T2WI **(A)** and axial T1WI (**B)** showing no significant abnormal findings. Axial FA map **(C)**, showing focal areas of reduced medullary FA values (white arrows), axial ADC map **(D)** showing focal areas of increased medullary ADC values (white arrows). Axial DTI b0 image **(E)**, medullary ROI is defined in the lower area of the right kidney showing the corresponding ADC value of 1.53×10^{-3} mm /s and FA value of 0.191. Fiber tractography reconstruction **(F)** The same ROI reveals a lower tract count with no evident directional alignment (white arrow). Axial DTI b0 image **(G)** medullary ROI is defined in the middle portion of the left

kidney, with corresponding ADC value of 1.48×10^{-3} mm /s and FA value of 0.154. Fiber tractography reconstruction **(H)** fiber tracking from the same ROI demonstrates fewer tracts, which lack preferential orientation (white arrow).

DISCUSSION

Diabetic nephropathy (DN), is emerging as a global public health concern related to complications of diabetes mellitus (DM), it is associated with alterations in renal morphology and physiological function, micro-albuminuria is one of diabetic nephropathy clinical signs [(9)].

Serum creatinine and eGFR are two test measures that are utilized for DN patient diagnosis, prognosis, and follow-up. However, these metrics lack specificity and sensitivity [(9)].

Recognizing the pathophysiological mechanisms behind kidney disease is possible by non-invasive advanced MRI techniques such as DTI, which mainly emphasize the structural as well as functional changes occurring in the renal tubules [(10)].

DTI is a non-invasive effective tool for assessing the micro-structural integrity of the kidney. Different kidney disorders had an impact on changes in DTI measurements. FA and ADC are two important rotationally invariant scalar metrics obtained from DTI.

The FA metric indicates how effectively diffusion tensor imaging can measure anisotropic diffusion. It is primarily influenced by the directional diffusion of water molecules in the renal medulla, resulting from the radial orientation of renal vessels and tubules, combined with micro-circulatory contributions to diffusion [(11)].

The purpose of this study was to assess the additional benefit of quantitatively analyzing DTI parameters for early detection of renal microstructural changes in type 2 DM patients, with a particular focus on differentiating between normo-albuminuria and micro-albuminuria stages using functional MRI with DTI.

Our study addressed that renal cortical FA values were the most sensitive marker, helps in distinguishing all studied groups, it increased with the progression of nephropathy/proteinuria. Cortical FA values differed significantly between control group and diabetic patients, reduced renal cortical FA in both diabetic groups suggests early micro-structural damage, even before overt albuminuria.

Medullary FA values were significantly reduced at micro-albuminuria patient group in comparison to control group that was supporting the theory of tubular damage.

The ADC values of the studied groups revealed that cortical ADC values can detect early changes in patient with micro-albuminemia as they revealed significant elevation in patients with micro-albuminuria when compared to patients with normo-albuminuria.

Elevated ADC in the cortex of micro-albuminuria patients may reflect early interstitial edema or inflammation. These changes correlate with the A/C ratio, supporting that DTI represents a promising non-invasive for early detection of diabetic nephropathy. There was no statistically significant differences as regard medullary ADC values among the studied groups, that suggests that medullary perfusion is preserved early in the process of the disease, These results align with those reported in the study of **Panduranga *et al.*** [(12)] who demonstrated a significant differences in both cortical and medullary FA values between healthy controls and diabetic subgroups in his study. Furthermore, it revealed that cortical ADC values were notably lower in diabetic patients compared to control group.

Our study's analysis of the diabetic groups showed that cortical ADC values decreased significantly ($p < 0.001$) as proteinuria severity increased, indicating a correlation with the progression of renal damage, that aligned with **Emre *et al.*** [(13)] who suggested that ADC values of the renal parenchyma may serve as a useful tool for both clinical staging and early diagnosis of kidney disease patients.

The outcomes for ADC and FA values in the DTI study conducted by **Feng's *et al.*** [(14)] were consistent with our results. Their data also suggested that FA may have greater potential than ADC in assessing water molecules diffusion of and identifying subtle microstructural alterations in human renal tissue.

As regard the correlation between DTI Parameters and clinical variables between the three studied groups the strongest correlations were between cortical FA Cortex and A/C ratio that was an indicator that albuminuria severity can predict micro-structural damage. The correlation between FA & ADC values with eGFR were moderate ($\rho = 0.47–0.52$ that) support DTI's role in functional assessment. While the weakest correlation was between HbA1c and both DTI metrics which suggested that glycemic control is less directly linked to micro-structural changes.

Mansour *et al.* [(15)] agreed with these results in his study; he reported that FA values of the renal cortex and medulla in CKD patients correlated significantly with serum creatinine and e-GFR indicating their potential as imaging markers for renal function.

Consistent with our findings, **Saini *et al.*** [(16)] found that in individuals with renal parenchymal disease, renal medullary FA had a substantial positive connection with e-GFR and a notable inverse correlation with serum creatinine ($r = -0.785$).

We observed that reductions of both FA & ADC values can reflect early micro-structural damage in the diabetic kidneys, as cortical FA could distinguish the three studied groups suggesting early changes even before albuminuria develops, so that it has a major role in early detection of the disease, while the progressive reduction in both values can mirror the worsening of albumineria. These results align with the earlier research conducted by **Razek *et al.*** [(17)] who found that the renal cortex's FA and ADC may be useful in

distinguishing diabetic kidney from healthy kidneys, predicting the occurrence of macro-albuminuria in diabetic patients, and showing correlations with certain laboratory biomarkers of diabetes.

Also **Ye *et al.* [18]** found in his study that early-stage CKD diabetes patients exhibited notably reduced FA values in the renal cortex and medulla.

As regards tractography, in our study, we noticed a statistically significant difference was found between microalbuminuric group in relation to other two groups, that was consistent with **Gaudiano *et al.* [19]** who found in his study that tractography revealed a number of patterns of disruption, ostensibly due to decreased directed diffusion: a seemingly smaller number of tracts, early interruption, and disorientation.

This study's primary limitation is the relatively small number of patients and control subjects; to address this, multicenter studies involving a greater number of cases are encouraged.

In summary, our findings indicate that DTI is a safe, non-invasive, and effective advanced MRI technique capable of detecting early renal functional and micro-structural alterations changes in patients with early DKD. Alterations in DTI parameters—such as FA, ADC, and fiber tract count and length—may serve as valuable indicators for identifying and monitoring early renal injury in individuals with T2DM.

CONCLUSIONS

DTI and tractography effectively detect early renal microstructural changes in diabetic nephropathy. Cortical FA is a sensitive biomarker for early dysfunction, showing strong diagnostic performance and correlation with renal function and albuminuria.

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