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Sonographic Assessment of Renal Changes in Adults with Diabetes Mellitus at Amana Regional Referral Hospital, Dar es Salaam, Tanzania

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Abstract

Introduction: Diabetic kidney disease is a common and morbid complication of diabetes mellitus patients and the leading cause of chronic kidney disease worldwide. It is probably the third most common cause of chronic kidney disease in Africa after hypertension and glomerulonephritis. Little has been researched on renal sonographic changes in these patients to predict chronic kidney disease in African settings. This work aimed to determine the prevalence of diabetic nephropathy in adults with diabetes and assess morphometrical changes of the kidneys using ultrasonography. We also aimed to determine the influence of age, sex, duration and type of diabetes and changes in biochemical parameters on kidneys disease in patients with diabetes.

Results: The prevalence of diabetic nephropathy was found to be 26.6%. There was no association between age or sex ($p>0.05$) and diabetic nephropathy. There was a significant association between the disease duration and type of diabetes mellitus on diabetic nephropathy ($p>0.005$). The study revealed a statistically significant association between biochemical parameters (proteinuria, serum creatinine and creatinine clearance levels) and changes in renal parenchymal echogenicity ($p<0.05$); for both right and left kidneys.

Conclusion: Renal parenchymal echogenicity on ultrasound was a good indicator of renal changes that may progress into DKD in a patient with diabetes.

Keywords: Ultrasonography; Diabetes Mellitus; Renal parenchyma echogenicity; Diabetic kidney disease

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Abbreviations

AKD: Acute Kidney Disease; CKD: Chronic Kidney Disease; DKD: Diabetic Kidney Disease; DM: Diabetes Mellitus; ESRD: End-Stage Renal Disease; HIV: Human Immunodeficiency Virus; GFR: Glomerular Filtration Rate; USG: Ultrasonography; RPT: Renal Parenchyma Thickness

Introduction

Diabetes mellitus (DM) is the typical cause of kidney disease worldwide; it may lead to several complications, including end-stage renal disease and cardiovascular diseases [1]. In some cases, even when diabetes is controlled, the disease can lead to Acute Kidney Disease (AKD) or may progress to Chronic Kidney Disease (CKD) and kidney failure [2]. It is approximated that 1 out of 4 adult patients with diabetes has Diabetic Kidney Disease (DKD) [3]. DKD affects about 15% to 25% of type 1 diabetic patients and 30% to 40% of patients with type 2 diabetes [4,5].

CKD screening in patients with diabetes is based on the Albumin excretion rate and the estimated Glomerular Filtration Rate (GFR) [6]. Other phenomena ensue earlier in the course of diabetic nephropathies, such as glomerular hyperfiltration, renal hypertrophy, and renal histological lesions [7]. However, their routine assessment in clinical practice is inconvenient: renal biopsies are invasive, GFR determinations are expensive, and GFR estimations do not help diagnose hyperfiltration.

Ultrasonography (USG) is the first-line imaging modality for evaluating CKD; it is non-invasive and relatively cost-effective compared to other radiological imaging techniques. Renal USG has replaced standard radiography and has become the standard imaging modality in investigating renal

diseases due to its non-invasive nature and easy availability [8,9].

Aim of the Work

This study aimed to evaluate renal changes in adults with DM by assessing morphometrical changes of the kidneys using ultrasonography. The current study also aimed at determining the influence of age, sex, duration and type of DM and biochemical parameters on kidney injury in DM.

Materials and Methods

This observational cross-sectional descriptive study was conducted at Amana Regional Referral Hospital, Dar es Salaam, Tanzania, for ten months, from June 2020 to March 2021. After obtaining written consent, one hundred and thirty-nine patients with type 1 or type 2 diabetes aged 20 years and above were recruited. Patients with or without any known diabetic renal diseases were recruited; they underwent an abdominal diagnostic ultrasound. Pregnant patients and patients who could not change posture for accurate assessment of kidneys during US examination were excluded from the study. Diabetic patients with co-HIV infection were excluded from the study to avoid overlapping HIV and diabetic nephropathy sonographic features. All the ultrasound examinations were performed using a real-time ultrasound machine modal HD5000 (Philips, The Netherlands) with a broadband curve-linear transducers of 2 MHz to 5 MHz frequency range.

Ultrasonographic parameters measured

Length of the kidneys: Bipolar renal length is accepted in the literature as a good indicator of renal size. To improve the differentiation of normal kidneys from those affected by chronic nephropathy, some authors have furthermore proposed evaluating renal volume using the ellipsoid formula (V= Craniocaudal diameter × anteroposterior diameter × transverse diameter × 0.5233) [10]. This formula indicates the appropriate renal volume with mean values of 231 ± 50.5 ml [11].

Parenchyma thickness: The mean values of parenchyma thickness with the duration of diabetes were calculated. From the literature, normal parenchyma thickness ranges from 1.5 cm to 2.0 cm [12,13].

Renal cortical echogenicity: From the literature, the average adult renal cortex is less echogenic than the adjacent normal liver. Using Hricak et al. [14] modified classification, visual grades interpretation was made by comparing the right kidney to the normal liver and left kidney to the normal spleen on the same scan. Renal echogenicity classification by modified Hricak et al. [15] is given as follows:

Grade 0: Normal renal echogenicity (lower than that of liver/spleen)

Grade I: The echogenicity of the renal cortex is equal to that of the liver/spleen

Grade II: The echogenicity of the renal cortex is greater than that of the liver/spleen but less than the renal sinus

Grade III: Echo intensity of the renal cortex was markedly increased and equal to that of the renal sinus.

When renal echogenicity was equaled to or greater than echogenicity of the liver indicates renal disease [14,15]. Images obtained were printed on thermal paper, qualitatively compared by two independent observers to minimize observer bias. The grade of echogenicity was observed and graded for each patient.

Biochemical parameters

Proteinuria: Proteinuria refers to the presence of any type of protein in the urine (e.g., albumin, globulins and mucoproteins); however, albumin is the predominant protein in the urine. Proteinuria can arise from different physiologic and pathologic causes, but persistent proteinuria associated with normal urine sediment is consistent with kidney disease. The urine dipstick colorimetric test was used for screening the detection of proteinuria.

Serum creatinine or calculated creatinine clearance: Both methods are the most convenient estimates of GFR, requiring only a single blood sample. As serum creatinine is highly dependent on age, sex and body size, several formulae have been developed to estimate the muscle mass and assumed creatinine production.

The most well-known formula is the Cockcroft-Gault formula, which is relatively simple and reasonably accurate. The average value is approximately 125 mL/min (75 Ml/min to 125 Ml/min). For women, the formula is multiplied above by 0.85. It is given as follows [16,17]:

$$\text{Creatinine Clearance (mL/min)} = \frac{140 - \text{age[yrs]} \times \text{Weight[kg]}}{\text{Serum creatinine (micromol/L)}}$$

Data analysis

Data collected were coded and analyzed using SPSS version 25. Statistical significance was tested using the Chi-square test. $p<0.05$ was considered significant.

Results

Demographic and clinical data

The mean age was 52.27 years (youngest 24 years, oldest 80 years). Seventy-two (72) patients were also suffering from cardiovascular disease (hypertension), and sixty-seven (67) was suffering from DM only. 35 (25.2%) patients had disease duration of fewer than five years, 48 (34.5%) had disease duration between 5 to 10 years, and 56 (40.3%) patients had disease duration of more than ten (10) years.

The proportion of patients with diabetic nephropathy

The proportion of patients with diabetic nephropathy by Age, Sex, type of diabetes mellitus and disease duration is summarized

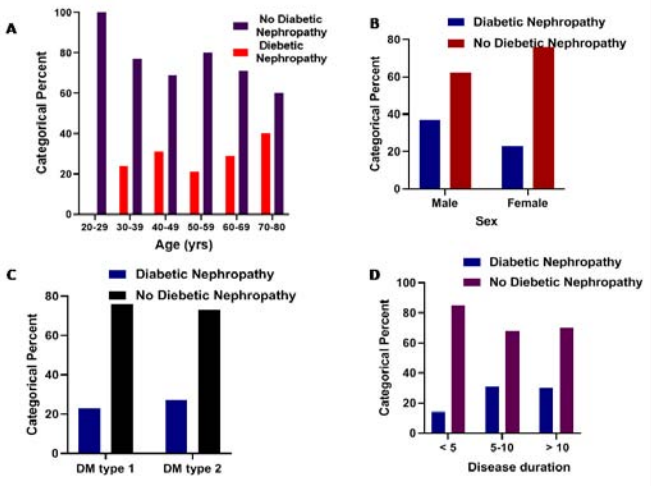

Figure 1: Proportion of patients with diabetic nephropathy. Categorical classification of patients with Diabetic nephropathy by age (A), sex (B), type of DM (C) and according to disease duration (D).

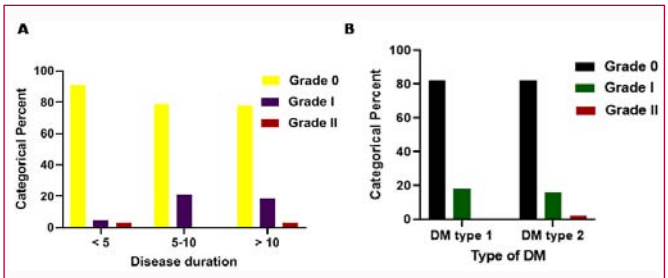

Figure 2: Proportion of renal parenchymal echogenicity according to the duration of disease (A) and type of DM (B)

in Figure 1 (N=139). High proportions of individuals with diabetic nephropathy were in the age group 70 to 80 years old (Figure 1A). Diabetic nephropathy in this age group was more pronounced in males than female population (Figure 1B)). Diabetic nephropathy was seen more in type 2 diabetes mellitus patients (Figure 1C); with more than five years (Figure 1D). There was no statistical significance between diabetic nephropathy and age, sex or type of diabetes mellitus (P- values >0.05). However, there was a statistical significance for diabetic nephropathy and disease duration (P value <0.0082).

Distribution of renal sonographic findings by duration and type of diabetes mellitus

Few patients showed reduced left kidney lengths with more than five years of disease duration. The reduction in kidney length was more prominent in DM type 2 than in DM type 1 patients. There was no significant reduction in kidney length with disease duration (p-values >0.05). The proportion of kidney length by duration and type of diabetes mellitus is summarized in Table 1 (N=139).

The proportion of renal parenchymal thickness by duration and type of DM

The result summarized in Table 2 depicts that as the duration of DM increases, the left renal parenchymal thickness decreases. Both right and left renal parenchyma thickness tend to decrease in DM type 2 only, and no observed changes in DM type 1. Nonetheless, the results were not statistically significant (P values >0.05).

Renal parenchymal echogenicity by duration and type of DM

The results showed that as the duration of the diabetic disease progresses (>5 years), there were a statistically significant proportion of patients presented with grade I renal parenchymal disease regardless of the types of DM (P=0.0061). Grade II renal parenchymal disease was only observed in DM type 2 (Figure 2A, 2B). There were no patients observed with grade II renal parenchymal disease. Figure 2 summarizes the proportion of renal parenchymal echogenicity

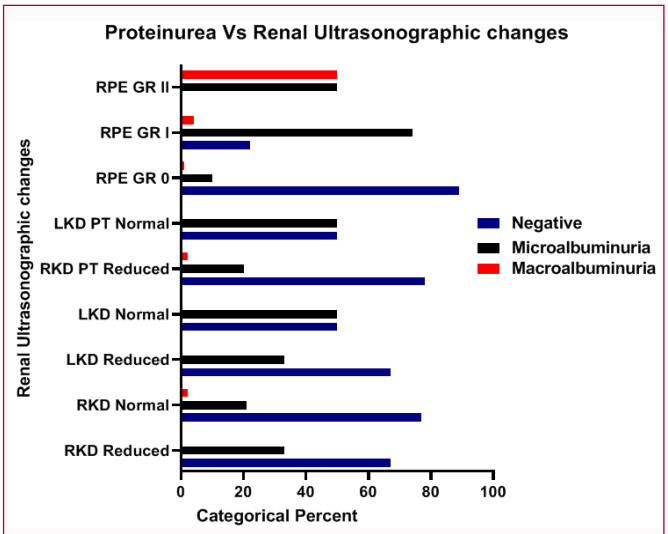

Figure 3: Relationship between proteinuria and renal ultrasonographic changes (N=139).
RPE: Renal Parenchymal Echogenicity; LKD PT: Left Kidney Parenchymal Thickness; RKD PT: Right kidney Parenchymal Thickness; LKD: Left Kidney Length; RKD: Right Kidney Length

according to disease duration and type of DM.

Biochemical parameters and renal ultrasonographic changes

Patients with microalbuminuria were also found to have reduced right and left kidney lengths and reduced and increased both right and left renal parenchymal thickness. 73.9% of patients who were found to have renal parenchymal echogenicity grade I presented with microalbuminuria. 50% of patients who presented with grade II renal parenchymal echogenicity had microalbuminuria, and the remaining fifty percent (50%) had macroalbuminuria. The results displayed a statistically significant association between proteinuria and renal ultrasonographical changes (P=0.0001). The relationship between proteinuria and ultrasonographic changes is displayed in Figure 3.

Patients with high serum creatinine levels were almost equal proportions of reduced right and left renal lengths, reduced left renal parenchymal thickness but with a high proportion of increased right kidney parenchymal thickness (p-values =0.0001). 21.7% of patients had renal parenchymal disease grade 1 (Figure 4).

As depicted in Figure 5, most of the patients who had reduced creatinine clearance levels showed a high proportion of reduced left kidney length than that of the right kidney (72.2% *vs.* 68.8%). Changes in both renal parenchymal thickness (reduced or increased) were seen with equal proportions in both kidneys with reduced or

Table 1: Distribution of renal sonographic findings by duration and type of DM.

Right kidney length			p-value	Left kidney length		p-value
Disease duration	Normal (n=123)	Reduced (n=16)		Normal (n=121)	Reduced (n=18)	
<5 yrs (n=35)	28 (80%)	7 (20%)	0.223	33 (94.3%)	2 (5.7%)	0.311
5-10 yrs. (n=48)	43 (89.6%)	5 (10.4%)		40 (83.3%)	8 (16.7%)	
>10 yrs. (n=56)	52 (92.9)	4 (7.1%)		48 (85.7%)	8 (14.3%)	
DM Type						
DM type 1 (n=17)	17 (100%)	0 (0.0%)	0.219	15 (88.2%)	2 (11.8%)	1
DM type 2 (n=122)	106 (86.9%)	16 (11.5%)		106 (86.9%)	16 (13.1%)	

Table 2: Proportion of Renal parenchymal thickness by duration and type of DM (N=139).

Duration	Renal changes					
	Right kidney parenchymal thickness			Left kidney parenchymal thickness		
	Reduced	Normal	Increased	Reduced	Normal	Increased
<5 yrs (n=35)	2 (5.7%)	31 (88.6%)	2 (5.7%)	0 (0.0%)	33 (88.6%)	2 (5.7%)
5-10 yrs (n=48)	4 (8.3%)	43 (89.6%)	1 (2.1%)	1 (2.1%)	46 (95.8%)	1 (2.1%)
>10 yrs (n=56)	3 (5.4%)	53 (94.6%)	0 (0.0%)	3 (5.4%)	52 (92.2%)	1 (1.8%)
	p=0.473			p=0.558		
Type of DM						
DM type 1 (n=17)	0 (0.0%)	17 (100%)	0 (0.0%)	0 (0.0%)	17 (100%)	0 (0.0%)
DM type 2 (n=122)	9 (7.4%)	110 (90.2%)	3 (2.5%)	4 (3.3%)	114 (93.4%)	4 (3.3%)
	p=0.731			p=1.000		

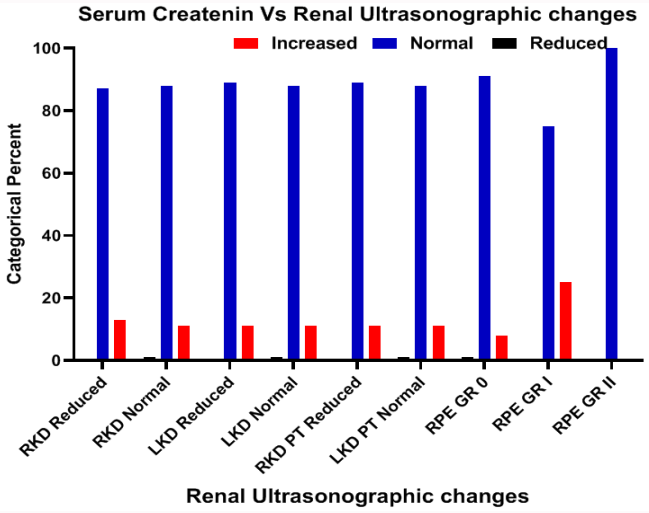

Figure 4: Relationship between serum creatinine and renal ultrasonographic changes.
RPE: Renal Parenchymal Echogenicity; LKD PT: Left Kidney Parenchymal Thickness; RKD PT: Right Kidney Parenchymal Thickness; LKD: Left Kidney Length; RKD: Right Kidney Length

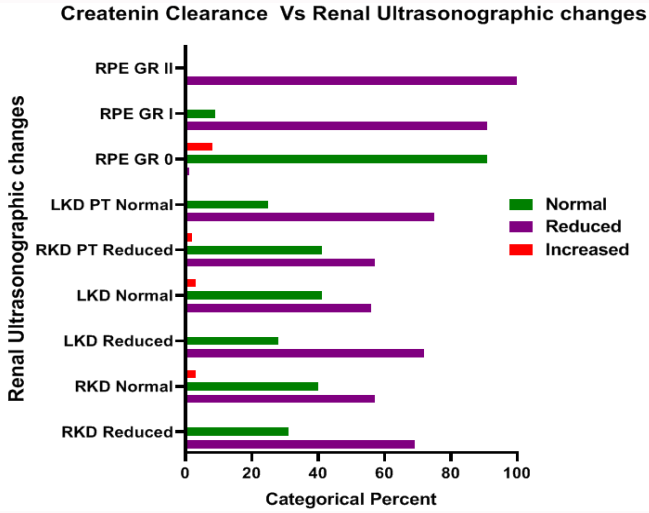

Figure 5: Relationship between creatinine clearance and renal ultrasonographic changes (N=139).
RPE: Renal Parenchymal Echogenicity; LKD PT: Left Kidney Parenchymal Thickness; RKD PT: Right Kidney Parenchymal Thickness; LKD: Left Kidney Length; RKD: Right Kidney Length

increased creatinine clearance (p-values >0.05).

However, reduced creatinine clearance level was highly associated with the grading of renal parenchymal echogenicity (p-value <0.0001).

Discussion

Ultrasound has been used extensively to build a relationship between renal parenchymal echogenicity patterns as a sonographic sign to many other variables like renal diseases histopathological pattern [18] and renal function variability [19]. The literature has well deliberated on the clinical manifestations of patients with DKD, including its potential causes and relationship to renal function parameters [20].

Renal structural changes are known to precede the development of proteinuria, hypertension, and reduced renal function in patients with DM. However, the determinants of these early structural changes are mainly unknown or asymptomatic. The basic fundamental theory in understanding the pathogenesis of DKD is the consequences of a series of specific progressive renal pathological changes that have their onset early in the course of diabetes [21]. These transformations develop during a long silent period, before features of clinical renal disease, including proteinuria, hypertension, and declining renal function [22]. Several studies have revealed no direct relationship between age or sex to the onset of DM complication [23,24].

There is limited research on renal sonographic changes in patients with DM living in Africa. A study conducted in Tanzania assessed sonographic renal changes (cortical volume and echogenicity) in patients with CKD regardless of the underlying disease. It was revealed that almost half of the patients with CKD had renal cortical volume below the typical healthy adult average [25]. They also observed that the severity of renal function impairment increased with an increase in renal echogenicity [26]. Zafer Saad revealed an increase in the mean values of some of the selected biochemical parameters in DM compared to the control group [27].

Findings from this study indicate that there is a slight decrease in left Renal Parenchyma Thickness (RPT) compared to the right kidney, but the difference is not statistically significant for both duration of disease and type of DM (P-values >0.05). It has been proposed that changes in RPT (increased or decreased) are more linked to an individual's genetic makeup than DM type [28]. In addition to the recognized and powerful effects of environmental factors, there is abundant evidence supporting genetic susceptibility to the microvascular complication of nephropathy in individuals with

both type 1 and type 2 diabetes and therefore influencing changes in renal parenchyma thickness[28]. Tarnoki et al. [29], provide a shred of evidence that unique environmental factors (e.g., lifestyle: Cigarette smoking, nutrition, lack of physical exercises) have an extraordinary influence (over 70%) in the loss of renal parenchyma of advancing age, which highlights the role of prevention of thin RPT.

The study revealed that most patients showed normal renal parenchymal echogenicity regardless of the disease duration (for both right and left kidney) or the type of DM (for both kidneys). The grade I echogenicity was more prominent, followed by grade II and none of grade III was observed during investigations. Furthermore, the finding indicates that none of the DM patients was found to have increased renal length for both kidneys for each type of DM, and there were no changes in biochemical parameters.

Our study shows a strong relationship between renal parenchymal echogenicity for both kidneys and proteinuria in patients with DM (P-value =0.0001). In addition to this, the data indicates a statistical significance for the relationship between serum creatinine level and serum creatinine clearance with increased renal parenchymal echogenicity; grade I was more prominent than Grade II in both cases (P-value <0.005). Chi. et al. [30] concluded a strong relationship between renal parenchymal echogenicity as a predictor of impaired relative renal function. They finally hypothesized that renal echogenicity at renal sonography might help determine which patients require more evaluation of renal function [30]. Our study has revealed similar findings.

Sommer et al. [31] reported that the creatinine levels showed a statistically significant correlation with renal parenchymal echogenicity grades (P value =0.001). They concluded that renal function changes paralleled changes in renal parenchymal echogenicity. Our study has revealed similar findings.

Therefore, based on the findings from this study, we can postulate that the increased renal parenchymal echogenicity on ultrasound is a good indicator of renal changes in a patient with DM disease. The presumption from these findings of changes in renal parenchymal echogenicity (renal parenchymal disease) detected ultrasonography might help decide which patients require the early clinical intervention of DKD by the nephrologists to prevent progression into End-Stage Renal Disease (ESRD).

Conclusion

Our results revealed that increased renal parenchymal echogenicity observed by ultrasound screening is a good indicator of renal changes in DM patients. Therefore, we suggest that DM patients undergo routine kidney screening by ultrasound and periodically monitor/assess for the levels of biochemical parameters; this may help decide which patients require the early clinical intervention of DKD by the nephrologists to prevent progression into ESRD.

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