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Research Article

Ultrasonographic Renal Dimensions Amongst Adult Nigerian Diabetics: Correlation with Clinical, Anthropometric and Metabolic Risk Factors

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ABSTRACT

Diabetes is now becoming a major public health problem globally. It is increasingly associated with renal diseases, particularly chronic kidney disease worldwide. A simple, accurate, reproducible and non-invasive method of evaluation is necessary for early morphological assessment for timely intervention, diagnosis, treatment, and evaluation of renal diseases in diabetes mellitus. In this cross-sectional comparative study, among one hundred and four adult diabetic cases and fifty-three healthy controls, the ultrasonographic renal dimensions were determined and compared in both cases and controls. Correlations were sought between the renal dimensions and the clinical, anthropometric, and metabolic characteristics of the study population. The dimensions of the kidneys in diabetic cases versus controls were; lengths (9.94± 0.76cm vs 9.27 ± 0.90 and 10.28 ± 0.87cm vs 9.41± 1.02cm(p=<0.001), cortical thickness (1.77± 0.28cm vs 1.26± 0.49cm, p<0.001 and 1.89± 0.52cm vs 1.37± 0.78cm, p<0.001 and volumes (121.9± 39.50cm3 vs 107.8± 29.82cm, p=0.026 and 136.3± 45.09cm3 vs 118.8± 33.79cm3, (p=0.015) were significantly higher in Diabetes mellitus cases on the right and left respectively. The waist circumference, fasting blood sugar, postprandial blood sugar, cholesterol, and urinary albumin, all had correlations with the mean kidney length. Taking together, the ultrasonographic renal lengths, cortical thickness, and volumes are increased in diabetic disease without renal function compromise compared to age-, gender- and body mass index-matched non-diabetic controls. The clinical, anthropometric, and metabolic parameters of the diabetes cases also showed significant correlations with mean kidney length.

Keywords: *kidney, ultrasonographic dimensions, Diabetes mellitus.*

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INTRODUCTION

Diabetes mellitus (DM), a metabolic disorder of multiple aetiologies characterized by hyperglycaemia from defects in insulin secretion, insulin action or both (WHO 1999; Pradeep 2010), has become a major public health concern globally (WHO 2015; Blas & Karup 2010; Chen et al, 2011), with serious socioeconomic burden from its management (Ala et al. 2013; Bommer et al, 2017). DM is one of the most complex chronic systemic diseases with long-term damage, dysfunction and failure of various body organs with about 1.5-2.2 million yearly deaths, mostly before the age of 70 years (WHO, 2016a).

In the developing countries, rapid urbanization, dietary changes, and increasing sedentary lifestyles are responsible for increased morbidity and mortality from DM (Frank, 2011), which in turn places huge financial stress on the already overloaded healthcare systems in Africa (Mbanya,2007). According to the diabetes country profiles, the prevalence of Diabetes in Nigeria is 4.3% (WHO, 2016), but varies from 0-2% in rural areas to about 5-11% in urban areas of Nigeria (Fasanmade and Dagogo-Jack, 2015).

Type 2 diabetes, which accounts for over 90% of Diabetes, have been reported to be more susceptible to different forms of both short- and long-term macrovascular, microvascular diseases and cancers (Larsson and Wolk 2011; Vigersky et al, 2011; Yanling Wu et al. 2014). Over the years, Diabetes and hypertension were both major risk factors for kidney disease (Jha et al, 2013). However, between 1990 and 2013 there was a decrease in the age-standardized rates for chronic kidney disease (CKD) due to hypertension by 22.4%, while the rates for CKD due to diabetes mellitus increased by 10.6% globally (Global Burden of Disease Study, 2015) which may be as a result of the continued increase in cases of Diabetes over the years. The effect of Diabetes on the kidneys is so serious that

about a third to half of the individuals with Diabetes develop kidney disease (Bakris 2011; Harjutsalo et al, 2014).

The prevalence of kidney diseases is on the increase in Sub-Sahara Africa this is projected to reach 34.3 million DM cases by the year 2040 from 14.2 million in 2015. Out of this number, Nigeria is said to account for 20% of all diabetes cases in the region (International Diabetes Federation, 2014). In addition to this high number of people with Diabetes in Nigeria is the problem of a high proportion of individuals with late diagnosis and those who remain undiagnosed or untreated (70-80%) (International Diabetes Federation, 2014; Oguejiofor et al., 2014; Fasanmade and Dagogo-Jack, 2015) as well as the increased cost of managing diabetic patients with renal impairment (WHO, 2016b).

Although laboratory parameters such as albumin excretion rate (AER) and the estimated Glomerular Filtration Rate (e-GFR) are employed in screening of chronic kidney disease in patients with Diabetes [Kramer and Molitch, 2005). Several researchers have reported that changes in the size and shape of the kidneys from diabetic kidney damage occur earlier than the AER and eGFR changes (Soheilipour et al, 2016; Premaratne et al. 2005; Fioretto et al, 2008). Also, the fact that kidney assessment in routine clinical practice may either involve invasive renal biopsies or expensive GFR determinations (Ibrahim et al. 2005; Chudleigh et al., 2007) has necessitated the use of a simple but cost-effective method, for early detection of morphological renal changes in diabetic patients in order to initiate timely intervention. An example is the estimation of kidney dimension, which is an important criterion in the diagnosis, treatment, and evaluation of renal disease (Muthusami et al., 2014). Although ultrasonography, computed tomography (CT) scan, magnetic resonance imaging (MRI) are the methods of choice in urological as well as nephrological practices currently (Moorthy and Venogopal, 2011), renal ultrasonography has emerged as a simple, affordable, reliable, ionizing radiation-free and non-invasive imaging technique compared to CT and MRI for routine clinical practice. This is because CT involves the use of ionizing radiation and contrast media for measurement of renal dimensions and MRI is very expensive and not readily available. Thus, this study aimed to evaluate renal dimensions in type two diabetes without CKD using ultrasonography and to seek correlations, if any, between the renal dimensions and selected Diabetes mellitus clinico-laboratory risk factors.

MATERIALS AND METHODS

Study design and setting: This was a cross-sectional comparative study design. Cases were recruited from the Endocrinology clinic of the University College Hospital (UCH), Ibadan, Nigeria, while controls were selected among non-diabetic, normotensive patients from the General outpatient's department of UCH and healthy volunteers, between July 2016 and April 2017. The UCH is a foremost tertiary referral hospital located in Ibadan, South-West of Nigeria.

Study population and sampling: Cases were adults aged 18 years and above who presented with symptoms and signs of Diabetes (polyuria, polydipsia, weight loss) that met blood sugar level criteria for Diabetes (random plasma glucose concentration $\geq$ 200mg/dl (11mmmol/l); fasting (>8hours) plasma glucose>126mg/dl(7mmol.l) and 2-hour postprandial glucose >200mg/dl during oral glucose tolerance test(American Diabetes Association, 2013). While healthy normotensive, non-diabetic adults, without renal or vascular diseases of similar age and socioeconomic status who had no symptoms and had normal range blood glucose levels were the control group. The controls were recruited from the GOPD University College Hospital and healthy volunteers.

Data collection and laboratory procedures: A pre-tested structured data form was administered to the participants at the time of recruitment. The socio-demographic data, weight in kilograms (kg), and height in metres (m) obtained using a stadiometer were recorded, and the BMI calculated as BMI= weight (kg)/height^2 (m^2) calculated. The participants' blood pressure measurement was done with an appropriate size cuff Mercury sphygmomanometer and recorded in mmHg. Information about the duration of type 2 diabetes mellitus was taken from the patients' clinical records. The relevant biodata and profiles above were documented in the datasheet.

Laboratory investigations carried out after an overnight fast for at least 8 hours and venous blood obtained for blood sugar (FBS) measurement on the morning of the renal dimension evaluation. Controls were screened for diabetes mellitus using the glucometer. Recent glycosylated haemoglobin and electrolyte and urea, as well as urinary albumin, were documented from the patients' case file. Blood samples were also obtained for serum lipids among the control and subjects. eGFR was calculated for each patient (KDOQI clinical practice guidelines, 2007).

Ultrasonographic procedures: All subjects had both kidneys scanned using a General Electric Logic P5 ultrasound scanner with a 2–5 MHz curved array transabdominal transducer. All participants were scanned in the supine and decubitus positions with the liver and spleen used as acoustic windows for the kidneys on the right and left, respectively. Each kidney was scanned in the longitudinal and transverse planes and the renal dimensions, length, width, anteroposterior diameter, and cortical thickness measured in centimeters. All patients were scanned by a certified radiologist while blinded to the laboratory test results.

The acquired measurements were recorded in a data form. Variables, data handling, and analysis on the kidney length, width, anteroposterior size, and cortical thickness were done using SPSS 23.0 statistical software (SPSS Inc. IL., USA). Kidney volume was estimated using the ellipsoid formula (Bauker *et al*, 1999).

Ethical considerations: Participation in the study was completely voluntary and based on written informed consent. Participants were made to understand that they were free to withdraw their consent at any time and that they will continue to receive a standard level of care, even in such a situation. The privacy of participants was maintained by using serial numbers on the case record forms. The study protocol was approved by the University of Ibadan/University College Hospital Ethical Review Committee with approval number UI/EC/15/0271.

RESULTS

One hundred and fifty-seven participants were recruited for this study, and about 66.2% (104) had Diabetes, while 33.8% (53) were normal. The mean age of the participants in the DM group was 59.9 ± 10.13 years with an age range of 34-84years, while the mean age for controls was 58.9 ± 9.5 years with a range of 38-80 years. Diabetes was highest among the age group 60 to 69 years (40.4%) followed by age group 50 to 59 years (27.9%). About 38% (20/53) of the controls were males while among the people with Diabetes 31% (32/104) were males. (Table 1).

Table 1:
Sex and Gender Distribution Of The Study Population

Variables	Control n (%)	Diabetic cases n (%)	p-value
Sex			
Male	20 (37.7)	32 (30.8)	
Female	33 (62.3)	72 (69.2)	0.380
Age groups			
Below 40 years	1 (1.9)	2 (1.9)	
40 - 49 years	11 (20.8)	16 (15.4)	
50 - 59 years	15 (28.3)	29 (27.9)	0.874
60 - 69 years	21 (39.6)	42 (40.4)	
70yrs and above	5 (9.4)	15 (14.4)	

There were significant differences between the waist circumference in the diabetic group (Mean = 92.73 ± 11.73cm) and the control group (Mean= 80.36 ± 8.20 cm) p <0.001. Similar significant differences were noted between the systolic and diastolic blood pressure p <0.001 respectively between participants with diabetes (Mean SBP = 127.9 ± 19.17 mmHg, Mean DBP= 77.46 ± 12.47 mmHg) and controls (Mean SBP = 109.0 ± 8.11 mmHg, Mean DBP = 71.92 ± 5.39 mmHg). The mean arterial blood pressure was significantly different in diabetics (Mean = 94.22 ± 13.54) than in controls (Mean = 84.30 ± 5.21) p <0.001. Also, the FBS showed statistically significantly differences in the diabetic group (Mean = 123.1 ± 25.06 mg/dl) compared to the control group (Mean = 80.85 ± 15.26 mg/dl) p <0.001. Likewise, diabetic participants had higher HbA_{1c} (Mean = 5.74 ± 0.84) than in the control group (Mean = 4.99 ± 0.36) p <0.001. Similarly, there was significant difference in serum creatinine between participants with diabetes (Mean = 1.3 ± 0.64mg/dl) and controls (Mean = 0.56 ± 0.26mg/dl) p <0.001. Furthermore, there was also statistically significant difference in the eGFR between diabetics (Mean = 70.59 ± 39.13mL/min/1.73 m^2) and controls (Mean = 130.57 ± 39.22 mL/min/1.73 m^2) p <0.001, as shown in Table 2.

Renal ultrasonographic measurement: The renal measurements showed significant differences among participants with diabetes' right and left kidney LS (Mean right kidney LS = 9.94 ± 0.76cm, Mean left kidney LS = 10.28 ± 0.87cm) and the control group (Mean right kidney LS = 9.27 ± 0.90cm, Mean left kidney LS = 9.41 ± 1.02cm) p<0.001.

Table 2:
Age, Clinical Factors And Biochemical Parameter Comparison Among The Control And Diabetic Group

Variables	Control group		Diabetic group		
	Mean	SD	Mean	SD	p-value
Age (years)	58.89	9.53	59.85	10.13	0.777
Waist circumference (cm)	80.36	8.20	92.73	11.73	<0.001
Systolic blood pressure (mmHg)	109.0	8.11	127.9	19.17	<0.001
Diastolic blood pressure (mmHg)	71.92	5.39	77.46	12.47	<0.001
FBS (mg/dl)	80.85	15.26	123.1	25.06	<0.001
HbA_{1c} (mg/dl)	4.99	0.36	5.74	0.84	<0.001
Serum creatinine (mg/dl)	0.56	0.26	1.31	0.64	<0.001
BMI (kg/m^2)	25.22	3.97	25.00	4.01	0.743
Mean arterial blood pressure (mmHg)	84.30	5.21	94.22	13.54	<0.001
eGFR ($ML/min/1.73m^2$)	130.6	39.22	70.59	39.13	<0.001

FBS = Fasting blood sugar; HbA_{1c} = Glycosylated haemoglobin; BMI = Body mass index; eGFR = estimated Glomerular filtration rate.

Table 3:
Renal Kidney Dimensions Among the Control And Diabetic Group

Variables	CONTROLS		DM PATIENTS		
	Mean	SD	Mean	SD	p-value
Right kidney LS (cm)	9.27	0.90	9.94	0.76	<0.001
Left kidney LS (cm)	9.41	1.02	10.28	0.87	<0.001
Right kidney AP (cm)	4.10	0.52	4.35	0.71	0.012
Left kidney AP (cm)	4.46	0.56	4.65	0.78	0.107
Right kidney cortical thickness (cm)	1.26	0.49	1.77	0.28	<0.001
Left kidney cortical thickness (cm)	1.37	0.78	1.90	0.52	<0.001
Right kidney volume (cm^3)	107.8	29.82	121.9	39.50	0.026
Left kidney volume(cm^3)	118.8	33.79	136.3	45.09	0.015
Right kidney TS (cm)	5.60	0.93	5.55	0.81	0.726
Left kidney TS (cm)	5.58	0.72	5.59	0.99	0.987

LS = longitudinal length; AP =Antero-posterior; TS = transverse; SD = Standard deviation.

Table 4:
Correlation Between Kidney Dimensions, Age, Clinical, and Laboratory Parameters among the Diabetic Cases

Variables	Kidney Length (cm)		Kidney volume (cm^3)		Kidney AP (cm)		Kidney cortical thickness (cm)	
	r	p-value	r	p-value	r	p-value	r	p-value
Age (years)	0.042	0.672	-0.099	0.333	-0.059	0.550	0.185	0.062
Waist circumference (cm)	0.227	0.020	0.144	0.157	0.119	0.230	0.180	0.069
Duration of DM	0.150	0.180	0.089	0.430	0.152	0.174	0.233	0.039
SBP (mmHg)	-0.183	0.063	0.046	0.104	0.167	0.090	-0.219	0.026
DBP (mmHg)	-0.211	0.031	-0.015	0.880	0.203	0.039	-0.189	0.056
FBS (mg/dl)	-0.236	0.016	-0.110	0.282	-0.077	0.434	-0.019	0.845
PPBS (mg/dl)	-0.293	0.003	-0.130	0.205	0.032	0.751	-0.172	0.084
Cholesterol (mg/dl)	-0.100	0.310	-0.055	0.593	-0.023	0.818	-0.079	0.430
HbA1c (mg/dl)	0.066	0.508	0.008	0.935	-0.054	0.585	0.319	0.001
Creatinine (mg/dl)	0.015	0.879	0.035	0.735	0.097	0.329	-0.064	0.522
UA (mg/dl)	-0.259	0.009	-0.067	0.522	0.100	0.321	-0.019	0.850
BMI (Kg/m^2)	0.033	0.742	-0.037	0.718	-0.011	0.915	0.047	0.636
MAP	-0.213	0.030	0.021	0.838	0.204	0.038	-0.221	0.025
eGFR (ml/min/$1.73m^{2)}$	0.081	0.419	0.092	0.370	-0.60	0.550	0.005	0.963

SBP=Systolic blood pressure; DBP=Diastolic blood pressure, HbA1c=glycosylated haemoglobin; UA=urinary albumin; MAP=Mean arterial pressure; eGFR=estimated glomerular filtration rate and r = Pearson's correlation coefficient.

The right kidney AP among diabetics (mean = 4.35 ± 0.71cm) had significant difference with the AP of the control group (mean = 4.10 ± 0.52cm). p= 0.02. There was also a statistically significant difference in the right kidney cortical thickness between participants with diabetes (mean = 1.77 ± 0.28 cm) and the controls (mean = 1.26 ± 0.49 cm) p<0.001. Likewise, participants with diabetes had significant thicker left kidney cortex (mean = 1.89 ± 0.52 cm) than the controls (mean = 1.37 ± 0.78 cm) p<0.001. Similarly, the right and the left kidney volumes were significantly different in the diabetic cases (mean right kidney= 121.90 ± 39.50cm^3; left kidney 136.31 ± 45.09cm^3), compared to the controls (mean = 107.81 ± 29.82cm^3; left kidney=118.82 ± 33.79cm^3) with a p value of 0.026 and 0.015 on the right and left respectively. (Table 3).
Comparing the renal dimensions in both sexes, only the right kidney AP showed significant difference between males (4.42 ± 0.73cm) and females (4.19 ± 0.62cm), p = 0.037. Other kidney measurements showed no significant differences, p>0.05. The male and female kidney dimensions are; right kidney LS= 9.72±0.85 cm and 9.71±0.88cm (p=0.977); left kidney LS = 10.07±0.98cm and 9.94cm±1.02cm (p=0.446); right cortical thickness =1.65±0.43cm and 1.57±0.44cm (p=0.298); left kidney cortical thickness =1.73±0.48cm and 1.72±0.75cm (p=0.927); Right kidney volume=123.2±42.77cm3 and 114±33.34cm^3(p=0.185); left kidney volume =131.9±37.94cm^3 and 129.3 ±44.10cm^3 (p=0.733).

Correlation of clinical and laboratory factors and renal dimensions: Table 4 showed that among patients with diabetes, waist circumference had a statistically significant correlation with the mean kidney length (r = 0.227, p=0.020). Likewise, the diastolic blood pressure had a statistically significant correlation with the mean kidney length (r = -0.211, p=0.031). MAP had statistically significant correlations with kidney length (r = -0.213, p=0.030). Among the laboratory parameters, the FBS had a significant correlation with mean kidney length (r = -0.236, p=0.016). Similar correlations were seen between the PPBS and mean kidney length (r = -0.293, p=0.003); as well as between the urinary albumin and the mean kidney length (r = -0.259, p=0.009). The cholesterol level, however, had no significant correlation with the kidney length (r = -0.100, p=0.310).

Furthermore, the kidney AP showed significant correlation with diastolic blood pressure (r = 0.203, p=0.039) and MAP (r = 0.204, p=0.038) respectively while the kidney cortical thickness had statistically significant correlation with duration of diabetes (r = 0.233, p=0.039), systolic blood pressure (r = -0.219, p=0.026), HbA1c (r = 0.319, p=0.001) and MAP (r = -0.221, p=0.025) respectively.

DISCUSSION

This hospital-based comparative study among type 2 diabetes patients with age, sex, and BMI-matched controls provides information about the association between certain physiological and biochemical variables, renal dimension, and Diabetes. Findings from this study showed an expected increase in the number of diabetic patients with increasing age and a peak in the age group 60 to 69 years. Fiagbe et al. (2017) reported a similar trend in their study among 210 participants (70 cases and 140 controls), in which about 61.4% of diabetic patients are 60 years and above.
This current study also showed the importance of certain physiological and biochemical factors as possible risk factors for Diabetes. Waist circumference, systolic blood pressure diastolic blood pressure, FBS (mg/dl), HbA1c (mg/dl), serum creatinine, and mean arterial blood pressure were significantly higher in patients with Diabetes than in the control group. At the same time, eGFR was significantly lower among patients with Diabetes compared to the control group. This is congruent with previous studies (González-Villalpando et al, 2014; Mitta et al, 2010; Madhusudan and Sadhvimani, 2017). Adebamowo et al. (2016) in their study on the impact of Type 2 diabetes on impaired kidney function in sub-Saharan African populations reported a higher level in serum creatinine among participants with type 2 diabetes (88.4 ± 44.2 µmol/l) compared to participants without type 2 diabetes (79.6 ± 17.7

µmol/l). Also, when eGFR was compared between the two groups in this study, it reported a lower mean eGFR for those with type 2 diabetes with a p-value <0.001. Likewise, similar to our findings, Hameed et al. (2017) reported that fasting blood glucose, systolic pressure, diastolic pressure, and HbA1c were significantly higher among diabetic patients compared to the control groups (p<0.001). Expectedly, the values of most of the physiological and biochemical variables in the diabetic group that showed a significant difference between diabetic patients and the control group in our current study were within a normal range since most of the diabetic patients were already under treatment. However, serum creatinine in the diabetic group was higher than the normal range (<1.20mg/dl). This may be an indicator of early-stage kidney diseases in diabetic patients. However, the mean eGFR of 70.59ml/min/1.73m^2 among the diabetes cases showed that the majority of these cases were not in the nephropathy range, usually describe as <60ml/min/1.73m^2 (Kramer and Molitch, 2005).

Renal dimensions except for left kidney AP and both kidney TS also showed a significant difference between the control group and diabetic patients in this present study. Patients with Diabetes had statistically significant higher renal length, cortical thickness, and renal volume compared to the control group, in keeping with renomegaly in the diabetic group. This result is similar to findings by previous studies that diabetes mellitus does not lead to a reduction in kidney sizes in its initial phase (Paivansalo et al, 1998; John et al, 2018; Mancini et al, 2013). Further analysis of the mean renal dimensions in our study showed that only the renal length was independently associated with Diabetes (AOR 16.69; 95% CI = 1.03, 132.3; p =0.047) which indicates that renal length may be an important determinant for Diabetes in our study population. Kidney damage is common among diabetic patients (Afkarian et al, 2016) and screening of Chronic Kidney Disease (CKD) in patients with Diabetes is based on the Albumin excretion rate (AER, threshold: 30 mg/24hours) and the estimated Glomerular Filtration Rate threshold of 60 mL/min/1.73 m^2 (Kramer and Molitch, 2005). However, several studies have reported a significant correlation between renal dimension and several indicators of kidney function, thereby regarding renal dimensions as important parameters in making an ultrasonographic diagnosis/ prognosis (El-Reshaid et al, 2014; Kariyanna et al, 2010; Korkmaz et al, 2018).

The left kidney dimensions were higher than that of the right kidney, in agreement with the findings of Saeed et al. (2012), and adduced to the fact that the smaller volume of the spleen on the left compared to the liver and the shorter and straighter left renal artery course causing increased blood flow results in larger growth of the left kidneys in the study population.

Also, findings from this study showed that renal length had correlations with more predictors of kidney function in a diabetic patient than other renal dimensions. This agrees with previous studies that renal length may be an important indicator of the prognosis and diagnosis of renal dysfunction (Sanusi et al, 2009). Other studies in diabetes have shown that the renal cortical thickness has a significant correlation with the glomerular filtration rate (Yamashita et al, 2015), and that, the HbA_{1c} shows long term assessment of glycaemic control (WHO, 2011; Modi, 2016). The correlation between cortical thickness, duration of Diabetes, and $HbA_{1c,}$ in this study, suggest that renal cortical thickness maybe an indicator of Diabetes chronicity and long-term compliance with diabetic control. Although in this current study, there was no significant correlation between renal dimensions and eGFR (Rigalleau et al. 2010). However, renal dimension had a significant correlation with fasting glucose, MAP and urinary albumin which is associated with eGFR/or kidney function (Wang et al, 2017; Sirivole and Eturi, 2017) which indicates that renal dimension may also provide information regarding disease progression or stability (Ali Omer et al, 2014; Zira, 2017).

In conclusion, the ultrasonographic renal lengths, cortical thickness, and volumes are increased in diabetic disease without renal function compromise compared to age-, gender- and body mass index-matched non-diabetic controls. The clinical, anthropometric, and metabolic parameters of the diabetes cases also showed significant correlations with left kidney lengths

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