Sonographic Evaluation of Renal Volume in Type 2 Diabetes Mellitus

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ABSTRACT

Background: Diabetic nephropathy (DN) is the leading cause of end-stage renal disease (ESRD) worldwide and it is estimated that more than 20% of type 2 diabetic patients may develop ESRD during their lifetime. **methods:** The study is a prospective ultrasonographic evaluation of kidney volumes in 228 adults with type 2 diabetes and 228 normal non-diabetic adult controls carried out at Aminu Kano Teaching Hospital, Nigeria from June 2015 to May 2016. The data were analysed using computer-based SPSS version 23 software for Windows. **Results:** The 228 patients with type 2 diabetes studied were composed of 120 (53%) females and 108 (47%) males with a mean age of 47.7years, (range 29– 67 years), while the 228 normal control group were composed of 108 (47%) females and 120 (53%) males with a mean age of 46.9 years, (range 28- 69years). The age difference between the study and control groups was not statistically significant (p=0.43). The mean renal volumes were significantly higher in the study group (114.10+3.97ml) compared to the control group (95.34+2.59ml); this was statistically significant (p=0.001). The mean renal volumes were higher in males compared to the females in both the study group and the control (p=0.001). The left mean renal volumes were higher than that of the right in both the study and the control groups (p=0.001). There was, however, no significant correlation between renal volume and BMI (p=0.086). **Conclusion:** The mean renal volume is significantly higher among diabetics compared with normal controls. Patients with Type 2 diabetes mellitus have no significant correlation between renal volume and BMI.

Keywords: Type 2 diabetes Mellitus, BMI, renal volume.

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Introduction

Type 2 diabetes is a metabolic disease that is characterized by hyperglycaemia (high blood sugar), in the context of insulin resistance and relative lack of insulin.[1] This is in contrast to type 1 diabetes in which there is an absolute lack of insulin due to the breakdown of islet cells in the pancreas.[2] The classical symptoms are excess thirst (polydipsia), frequent urination (polyuria), and constant hunger (polyphagia). Type 2 diabetes makes up 90% of cases of diabetes, with the other 10% due primarily to type 1 and gestational diabetes.[1]

Type 2 diabetes is primarily due to lifestyle factors and genetics.[3] Many lifestyle factors are known to be important to the development of type 2 diabetes, including obesity (defined by a body mass index of greater than 30kg/m^2), lack of physical activity, sedentary lifestyle, stress, and urbanization.[4] Excess body fat is associated with 30% of cases of Type 2 diabetes in people of Chinese and Japanese descent, 60-80% of cases in those of European and African descent, and 100% of Pima Indians and Pacific islanders.[5]

Dietary factors also influence the risk of developing type 2 diabetes. Consumption of sugar-sweetened drinks in excess is associated with increased risk.[3,4] Dairy fats and trans-fatty acids are known to increase

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the risk while polyunsaturated and monounsaturated fat decrease it.[3] A sedentary lifestyle is also believed to cause 7% of cases.[6]

Diabetes mellitus is characterized by recurrent or persistent hyperglycaemia and is diagnosed by demonstrating any one of the following: Fasting plasma glucose level ≥ 7.0mmol/L(126mg/dl), Plasma glucose ≥ 11.1mmol/l(200mg/dl) two hours after a 75g oral glucose tolerant test, Symptoms of hyperglycaemia and random plasma glucose ≥ 11.1mmol/L(200mg/dl), glycated haemoglobin (HbA1C) ≥ 6.5%.[6]

In sub-Saharan Africa, the prevalence and burden of Type 2 diabetes are rising quickly. The increase presents a substantial public health and socio-economic burden in the face of scarce resources. The rate of undiagnosed diabetes is high in most countries of sub-Saharan Africa, and individuals who are unaware they have the disorder are at very high risk of chronic complications.

In conjunction with the increase in Type 2 diabetes, a dramatic increase in the prevalence of diabetic nephropathy has been noted as a major complication that culminated into the most common cause of end-stage kidney disease.[7,8] In the elderly, diabetic nephropathy (DN) accounts for no less than 46% of chronic kidney disease.[9]

Diabetic Nephropathy (DN) is a clinical syndrome characterised by persistent albuminuria, a relentless decline in the glomerular filtration rate (GFR) progressing to end-stage renal disease (ESRD), raised arterial blood pressure, and enhanced cardiovascular morbidity and mortality.[10]

Glomerular hyperfiltration is the basic pathophysiology of diabetic nephropathy which often leads to intraglomerular hyperfiltration. The progression from hyperfiltration leads to the stage of basement membrane thickening. This is the earliest detectable change in the course of DN followed by expansion of mesangium and finally by nodular sclerosis. At this stage, the kidney may leak more serum albumin (plasma protein) than normal in the urine (albuminuria) and this can be detected by ordinary urinalysis techniques.

Given clinical management, hyperfiltration is not a parameter of practical value for the daily management of patients because it is too problematic to measure, whereas kidney volume measurement could be a potential tool for early identification of DN.[11]

Various imaging modalities have been used for renal volume estimation and are all fraught with prediction errors.[12] At present, ultrasonography is the imaging modality of choice for measuring renal volume.[13] Despite the prediction error, the ultrasound estimation of renal volume using the ellipsoid formula is more commonly employed because it is simple, reliable, non-invasive, uses non-ionizing radiation, reproducible, and does not require the use of an intravenous contrast medium.[14,15] It is readily available, affordable, offers excellent anatomical details, and requires no special preparation of patients.[12] Though underestimation of renal volume when compared with measurements by computed tomography and magnetic resonance imaging is a limitation notwithstanding, it is widely accepted and considered as the tool of choice especially where repeated examinations are required.[16,17,18]

Ultrasound has a great role in diabetic patients to predict the level of nephropathy and exclude other renal diseases apart from DN like chronic glomerulonephritis and ischaemic nephropathy.[19] Type 2 DM is the leading cause of ESRD worldwide especially with a longer duration of diabetes.[20] Thus, this study aims to establish the role of ultrasound in the evaluation of renal volume in patients with Type 2 diabetes mellitus and its correlation with age and BMI.

Method

Study Design

This is a prospective hospital-based cross-sectional study that determines the renal volume in 228 patients with type 2 diabetes (study group) as well as 228 normal non-diabetic adults (control group) aged between 18 to 69 years at Aminu Kano Teaching Hospital between June 2015 and May 2016.

Study population

Subjects recruited in this study included adults aged between 18 and 69 years of both sexes seen at the diabetic clinic of Aminu Kano Teaching Hospital (AKTH), with the diagnosis of type 2 diabetes without any known background renal parenchymal pathology. The control group constituted matched healthy non-diabetic individuals referred to the radiology department of AKTH for investigations of non-renal conditions.

Inclusion criteria for the study group

1. Adults with laboratory-confirmed type 2 diabetes
2. Adults with type 2 diabetes aged 18 to 69 years (The upper limit of 69 years was set to limit bias that may arise from the normal ageing process)

3. Those who willingly consented to participate in the study

Exclusion criteria for the study group

1. Individuals less than 18 years and individuals who are 70 years and above
2. Patients with type 2 diabetes who do not give informed consent for the study
3. Individuals with established congenital disease of the renal system such as
    a. renal ectopia
    b. multi-cystic dysplastic kidneys
    c. polycystic kidney diseases etc
4. Individuals with any of the following known causes of kidney disease or established kidney disease unrelated to diabetes
    i. Hypertension
    ii. Glomerulonephritis
    iii. Pyelonephritis
    iv. Obstructive renal diseases such as pelvic-ureteric junction obstruction, obstructive ureteric calculus, bladder outlet obstruction, etc.
5. Patient with intra-abdominal masses or malignancies with obstructive renal effects

Inclusion criteria for the control group

Healthy adults aged 18 years to 69 years of age and gender-matched visiting the radiology department for other investigations.

Exclusion criteria for the control group

1. Individuals with confirmed diabetes mellitus (DM)
2. Others as for the study group.

These conditions were excluded by obtaining a thorough history from the participants, and a review of the clinical records of the diabetic patients. Blood pressure was also taken to exclude hypertension. Congenital or acquired renal pathologies like hydronephrosis, hydroureteronephrosis, polycystic kidney, ectopic kidney, and pyelonephritis were excluded in the course of data collection by use of ultrasonography.

Ultrasound technique

All subjects who freely gave informed consent and signed up to be enrolled in the study had their ages, sex, weight, and height taken and BMI calculated. The participants' ages were obtained through history taking and cross-checked from the patients' case file/request cards. The heights were measured using a vertical height measuring scale calibrated in centimeters.

The weights were measured using a digital weighing machine. The BMI was calculated using the formula: weight (in kilograms) over height squared (in meters) i.e. k/m^2. The control individuals were mostly individuals sent to the radiology department for other investigations and healthy volunteers.

To ensure adequate compliance with inclusion and exclusion criteria, brief clinical history (such as history of hypertension, and stage renal disease) and physical examination (such as blood pressure) of subjects were taken.

All the diabetic subjects' hospital case files were cross-checked after obtaining approval from the medical records department, to ascertain their renal biochemistry status.

Each of the subjects was psychologically reassured and the procedure was comprehensively explained.

Subjects were scanned using a real-time, greyscale Mindray D-6 Schenzen China ultrasound machine which has a 3.5-5MHZ curvilinear transducer equipped with electronic calipers.

The scanning was carried out by the author under the supervision of a consultant in the department to ensure the validity of the measured renal dimensions.

Both kidneys were scanned following the liberal application of coupling gel to displace air from the skin surfaces.

The right kidney was scanned through the left posterior oblique or the left lateral decubitus position by scanning through the anterior axillary line intercostally or sub-costally, while the left kidney was scanned through the right posterior oblique or the right lateral decubitus position by scanning through the anterior axillary line intercostally or sub-costally.[22]

The liver and spleen served as acoustic windows on the right and left respectively, and also scanned posteriorly in the prone position.

Longitudinal scans of both kidneys were carried out with the patient in the prone position and the superior and inferior poles were identified and marked. The renal length (L) (in cm) was taken as the longest distance between the poles (bipolar length).

The anteroposterior diameter (AP) (thickness; T) (in cm) was also measured on the longitudinal scan, with the maximum distance between the anterior and the posterior walls of the kidney in the middle as illustrated in Fig. 1

The renal width (W) (in cm) was measured on the transverse scan as shown in Fig 1.

The renal hilum was identified and the transverse diameter was measured at this point. Renal volume was calculated using the ellipsoid formula; Length × Width × Thickness × π/6 where π/6 = 0.523.[23]

Laboratory Methods

- All laboratory information was obtained from the patient's case files.
- The latest fasting plasma glucose level of all subjects was recorded to ascertain their level of glycaemic control.
- WHO definition of diabetes mellitus as demonstrating a fasting plasma glucose level of ≥7.0mmol/l (126mg/dl) was used to diagnose patients as diabetics.
- The albuminuria status of each subject was recorded following urinalysis. This was defined according to the standards of medical care of the American Diabetes Association as:

Normal (<30mg/mg)
Micro albuminuria (30-299mg/mg)
Macro albuminuria (≥300mg/mg)

Data Management and Statistical Analysis

All sonographic parameters, laboratory data, and clinical data were collected using a structured data collection sheet and the findings were entered into a computer Excel spreadsheet. Statistical analysis was performed using the statistical package for social sciences (SPSS) for Windows (SPSS Inc, USA) version 23. Variables were presented as mean ± SD. A p-value of less than 0.05 was considered to be statistically significant.

Student's t-test was used to test the difference in means between variables. Regression analysis was used for the evaluation of the correlation between renal volume and duration of DM.

Ethical Consideration

Clearance from the Ethical Committee of Aminu Kano Teaching Hospital Kano was obtained before the commencement of the study with registration number NHREC/21/08/2008/AKTH/EC/1450.

Results

Demographic and clinical characteristics of the study population

A total of 456 subjects comprising 228 Type 2 diabetic subjects as well as 228 age and sex-matched controls were studied.

There was a slightly higher number of female subjects in the study group who constituted 53% (120 out of 228) while the males constituted 47% (108 out of 113) as shown in Fig 2. This difference however was not statistically significant (p=0.43). The distribution of individuals sampled as the control group for the study was also nearly even between the sexes. Although males were slightly higher constituting 53% of all individuals sampled (i.e. 120 of 228 individuals) while females made up 47% (i.e. 108 of 228 individuals) (Fig. 2). This difference was also not statistically significant (p=0.43). The ages of male patients in the study group ranged from 29-67 years with a mean of 47.7±10.7 years while those of the female patients ranged from 28- 69 years with a mean of 46.9±10.9 years (Table 1). There was no significant statistical difference between the mean age of male and female patients in the study group (P=0.49).

The ages of male subjects in the control group ranged from 31-69 years with a mean of 47.1±10.4 years while the age of the female subjects in the control group ranged from 28-69 years with a mean of 47.8±10.3 years. (Table 1) There was no significant statistical difference between the mean ages of male and female subjects in the control group (P=0.43).

The mean age of the study group was 47.70 +10.84 years while that of the control group was 46.86 + 10.33 years. There was no significant difference between the mean ages of the subjects and the control groups (p=0.46). The age distribution of the study and control groups is depicted in Fig 3.

The BMI of male patients in the study group ranged from17.1- 31.6kg/m^2 with a mean of 24.2 ±4.5 kg/m^2, while the BMI of female patients in the study group ranged from 16.6-40.2kg/m^{2}with a mean of 27.7±5.0kg/m^2. The BMI of the male subjects in the control group ranged from 16.9-33.3kg/m^2 with a mean of 23.6±5.3 kg/while the BMI of female subjects in the control group ranged from 15.0- 36.6-kg/m^2 with a mean of 23.6 ± 5.3kg/m^2. (Table 2).

The mean BMI of the study group was 25.96 + 4.76 kg/m^2 while that of the control group was 23.61 + 5.30 kg/m^2. This difference was not statistically significant (p=0.43).

Renal volume related significantly with the sex of individuals sampled ($p < 0.001$) with diabetic males having higher mean renal volume as compared to diabetic females.

($p < 0.001$) (Fig. 3). However, there was no statistically significant relationship between renal volume with age ($p = 0.875$) and BMI ($p = 0.877$) of individuals in the study population.

Generally, in both males and females combined, there was a significant difference between right renal volume (Rvol) and left renal volume (Lvol) in diabetic patients ($p < 0.001$) with left renal volume being larger than right. (Table 3) The left renal volume in diabetic males also were significantly larger than the right renal volume ($p < 0.001$). Similarly, in diabetic females left renal volume was larger than the right renal volume ($p < 0.001$). For the control subjects, renal volume in males was also significantly higher than that of females ($p = 0.001$), with the left renal volume being larger than the right in both sexes (Table 4).

There was no statistically significant relationship between BMI and right renal volume in diabetic males ($p = 0.086$). Similarly, BMI did not correlate significantly with right renal volume among diabetic females ($p = 0.604$). Also, in the control group, BMI did not have a significant correlation with right renal volume among male subjects.
($p = 0.913$). However, BMI related significantly to right renal volume among female subjects of the control group ($p < 0.001$) Fig. 4 and 5).

Table 1: Tabular Age distribution of the Study and Control Groups

Group	Sex	Lowest age	Highest age	Mean ± SD
Study Group	Male	32	67	48.29± 10.70
	Female	29	67	47.10 ± 10.98
Control Group	Male	31	69	46.62± 10.35
	Female	28	69	47.10± 10.30

Table 2: **Tabular presentation of BMI range and mean for Study and Control Groups**

Group	Sex	Lowest BMI	Highest BMI	Mean ± SD
Study Group	Male	17.10	31.55	24.22 ± 4.48
	Female	16.61	40.15	27.69± 5.04
Control Group	Male	16.85	33.27	23.59± 5.34
	Female	15.03	36.63	23.63± 5.26

Table 3: Comparison of Lvol and Rvol in both sexes of diabetic individuals

Sex	Mean Lvol± S.D.	Mean Rvol± S.D.	P
Males	155.41 ± 7.18	128.54 ± 5.23	< 0.001*
Females	115.78 ± 6.10	101.35 ± 5.40	< 0.001*

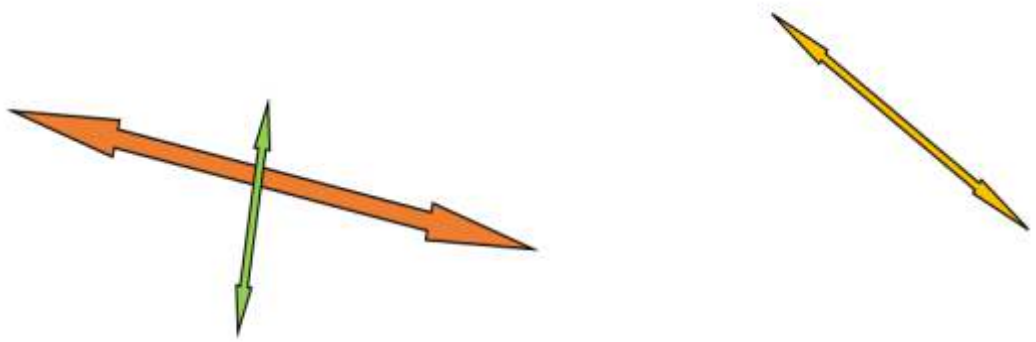
Average	134.37 ± 5.01	114.10 ± 3.97	< 0.001*

* = significant at 0.05 level

Table 4: Comparison of Lvol with Rvol in sexes of the Control group (Paired Samples test)

Sex	Mean Lvol± S.D.	Mean Rvol± S.D.	P
Male	120.59 ± 3.32	103.55 ± 3.78	< 0.001*
Female	139.53 ± 26.06 ±3.09	86.78	0.041*
Average	129.56 ± 12.52 ±2.58	95.61	0.006*

*=significant at 0.05 level (Paired Samples test)



A (Longitudinal Scan) **B (Transverse Scan)**

Fig 1: Sonograms obtained with the patient in a prone position showing measurements of renal dimensions (in cm). Longitudinal scan showing Renal length (L); Red arrow, and renal thickness (T); Green arrow. B-Transverse scan showing renal width (W); Yellow arrow

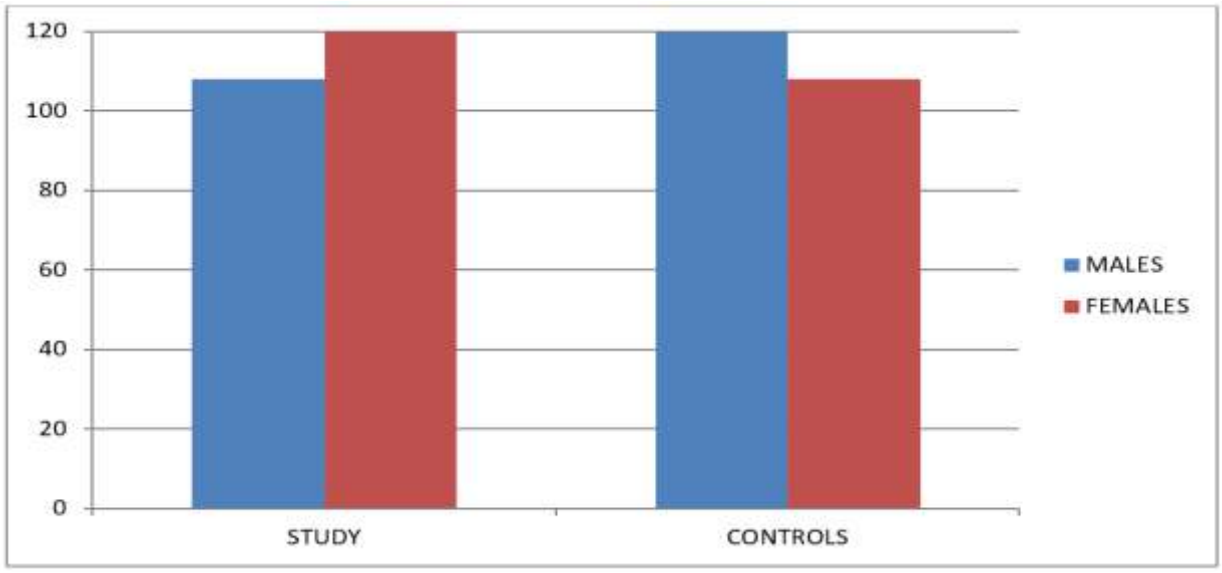


Fig. 2: Bar charts showing the sex distribution of study and control groups

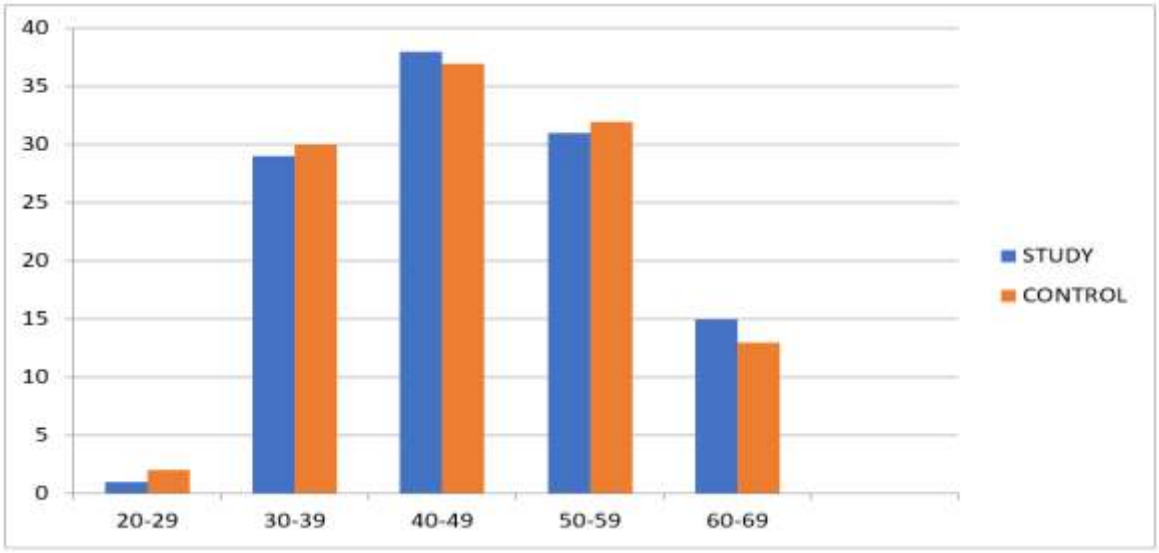


Fig. 3: Bar Chart Showing Age distribution of both study and control groups

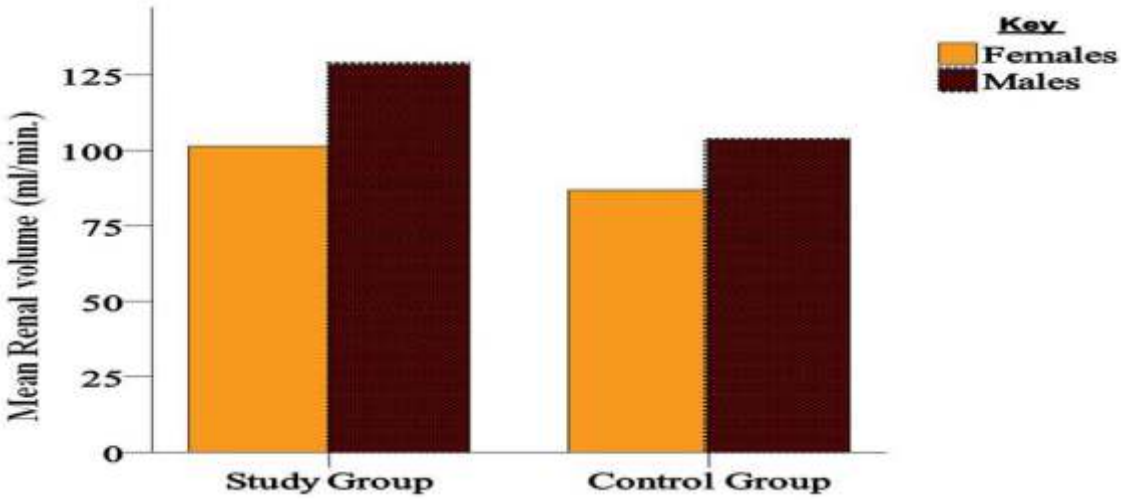


Fig. 4: Bar chart presentation of renal volume between study and control groups

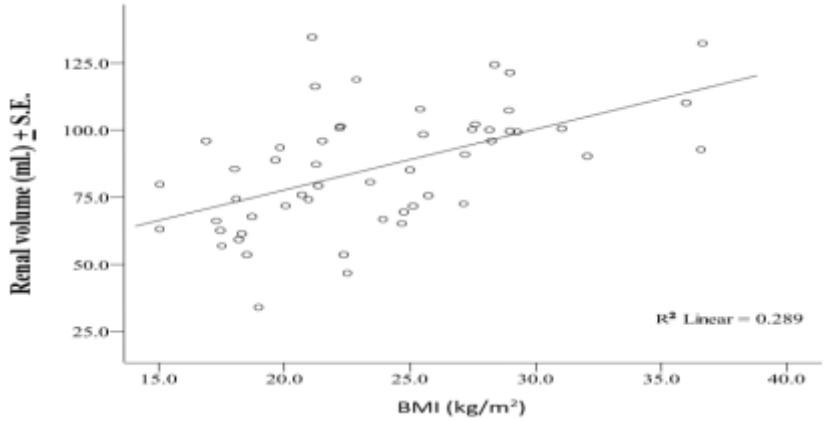


Fig. 5: Scattergram Showing Relationship between Rvol and BMI in control group females

Discussion

There were more females found with diabetes mellitus (53%) compared with males (47%) in this study. This is concordant with the findings of Chukwu et al.[24] in Enugu, Chinenye et al.[25] in Kano, and Zafar et al.[26] in Pakistan who found more females affected with diabetes than males. There was no significant statistical difference between the number of male and female diabetics. (p=0.43). Similarly, Chineye et al.[25] also did not find a significant statistical difference between the number of female and male diabetics.

The peak age group of the subjects with diabetes mellitus in this study was within the range of 40 – 49 years. This was found to be higher than the 34 – 36-year range in the study by Mumtaz et al.[27] in Pakistan. This difference may be a result of the disparity in diet and lifestyle of Nigerians and Pakistanis. The mean age of the study group was 47.7±10.9 years. This was similar to the report by Nyenwe et al.[28] in Port Harcourt who found a mean age of 49.5 years. This is slightly lower than the findings of Chinenye et al[25] who found a mean age of 57.1±12.3 years. This slight difference could be accounted for by the difference in the sample sizes of both studies. The sample size in this study was significantly lower than that of Chinenye et al.[25]

Among the study group, the mean age for males and females is 48.3±10.7 years and 47.1±10.9 years respectively. This is similar to the findings of Nyenwe et al.[28] in Port Harcourt who found the mean age of male diabetics to be 50.3 years and 47.6 years for females.

The higher mean renal volume in the study group (101.4±5.4ml) compared to that of the control group (128.5±5.2ml) in this study is similar to the findings of Zerbini et al.[29] in Milan Italy, Ruggenenti et al.[30] in Bergamo, Italy and Vincent et al[31] in de Bordeaux, France. Similarly, the statistically significant difference noted between the mean renal volume amongst the female diabetics compared to the female controls (p=0.015) and amongst the male diabetics compared to the male control group (p≤0.001) is similar to the findings of Zerbini et al.[29] Ruggenenti et al.[30] and Vincent et al. respectively[31]. The mean renal volume for the control group in this study on the left and right sides (129.6±12.5ml and 95.6±2.6 ml respectively) is similar to the findings of Ma'aji et al.[32] in Sokoto, who found mean renal volumes of 119.7±32.8 ml and 109.6±29.3 ml, with the left kidney larger than the right. The findings are also comparable to the report by Justo et al.[33] in Mexico, who also found that the left kidney is larger in the normal healthy adult population. This can be explained by the relatively smaller size of the spleen compared to the liver which allows the left kidney more space for growth; as well as the fact that the left renal artery is shorter and straighter than the right thereby, allowing increased blood flow in the left artery with a resultant relative increase in left renal volume.[33]

This study also showed that the renal volume relates significantly only with the sex of individuals sampled ($R^2 = 0.104$, $p < 0.001$) but not with age. Diabetic males had higher mean renal volume as compared to diabetic females. Emamian et al.[34] also found a similar positive correlation between renal volume and sex.

In this study, it was noticed that male subjects had larger renal volumes and similar findings were reported by Okoye et al.[35] in Southeastern Nigeria and Kang et al.[12] in Kangnam, South Korea. Renal volume has been found in studies by Brandt et al.[15] and Okoye et al.[35] in Southeastern Nigeria to positively correlate with height, weight, and body surface area. Furthermore, Adeela et al.[23] in Johor, Malaysia reported slightly larger renal sizes in males in their comparative study on renal sizes among different ethnicities. Similarly, Emamian et al,[34], and

Raman et al.[36] in Portsmouth United Kingdom, also reported that kidneys are larger in males than in females.

This study showed no significant relationship between renal volume and BMI. Studies have reported that both kidney volume and length were significantly correlated with all body indices (height, weight, and surface area).[37] Body weight showed the best correlation with right kidney dimensions, whereas BMI and age showed weak correlations with body indices.[38] Gavela et al.[39] reported a good correlation between kidney parameters and body parameters, with height exhibiting the best correlation. Cheong et al.[40] in Houston, found no correlation between kidney volume and BMI, height, or weight. Previous studies have shown that the kidney becomes relatively shorter and thicker with age.[41] However, no significant correlation was found in this study between renal volume and age because the patients are mostly below 50 years of age. A significant change in renal volume is seen mostly after 70 years.[32] A study by Emmamian et al.[34] reported that kidney size decreasing with age is almost entirely due to parenchymal reduction. The index study showed no significant relationship between renal volume and BMI thus agreeing with the findings of Cheong et al.[40]

Conclusion

This study established values of renal volume in patients with type 2 diabetes. The mean renal volume for male diabetics was higher than in females. The renal volume for normal individuals was also found to be higher in males than in females. The mean renal volume is shown to be significantly higher among diabetics compared with normal controls. Renal volume was generally found to be larger on the left than on the right side. Renal volume showed no significant positive correlation with age and BMI.

Renal volume was significantly higher amongst subjects with type 2 diabetes compared to their controls. Therefore, routine requests for renal scans which are relatively cheap and readily available for diabetic patients would help to mitigate the death toll from end-stage renal diseases caused by type 2 diabetes mellitus.

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Conflict of Interest Statement

The authors declared they do not have anything to disclose regarding the conflict of interest in this manuscript.

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