Renal cortical thickness and bipolar renal length and their correlation with estimated glomerular filtration rate of chronic kidney disease patients: a study at a teaching hospital in Ghana

Authors

Raphael Nicholas Mayeden[1], Klenam Dzefi-Tettey[2], Yaw Boateng Mensah[2], Benard Ohene-Botwe[3], Franklin Acheampong[4], Linda Nketiah[5], Ebenezer Ekow Dadson[6], Samuel Kwaku Obeng[7]

Affiliations

[1] Department of Radiology, School of Medicine, University of Health and Allied Sciences, PMB 31, Ho, Ghana

[2] Department of Radiology, Korle Bu Teaching Hospital, Korle Bu, P.O. Box KB 77, Accra, Ghana

[3] Department of Midwifery & Radiography, School of Health & Psychological Sciences, City University of London, Northampton Square, EC1V 0HB London, UK

[4] Korle Bu Teaching Hospital, Korle Bu, P.O. Box KB77, Accra, Ghana

[5] Department of Radiology, University of Ghana Medical Centre LTD, P.O. Box LG 25, Accra, Ghana

[6] Department of Radiology, Komfo Anokye Teaching Hospital, P.O. Box 1934, Adum, Kumasi, Ghana

[7] Research and Statistics Unit, Minerals Commission, #12 Switchback Road Residential Area, P. O. Box M248, Accra, Cantonments, Ghana

ABSTRACT

BACKGROUND: Chronic kidney disease (CKD) is progressive, requiring constant monitoring to inform aggressive therapy that halts disease progression. Besides laboratory tests, ultrasound is safe, inexpensive, and ubiquitous, and can be used to monitor CKD patients non-invasively. Several studies have tried to correlate ultrasound parameters like renal bipolar length (BPL) and renal cortical thickness (RCT) with estimated glomerular filtration rate (eGFR) among CKD patients with varied conclusions. No such study has been conducted in West Africa.

AIM: To determine the correlation between sonographically measured BPL and RCT with eGFR among adult CKD patients at a teaching hospital in Ghana.

MATERIALS AND METHODS: Ninety-nine eligible CKD patients were consecutively sampled. Greyscale abdominal ultrasound scans were performed with a Toshiba Aplio 300 ultrasound machine to determine BPL and RCT. The eGFR was computed using the Modification of Diet in Renal Disease (MDRD) formula. Correlations between eGFR, BPL and RCT were computed using Spearman's rank correlation and linear regression analysis.

RESULTS: Mean BPL, RCT and eGFR were 9.4±1.0cm, 6.6±1.4mm and 42.8 mL/min/1.73m^2, respectively. eGFR showed statistically significant correlation between BPL (ρ=0.406, p-value=0.001) and RCT (ρ=0.270, p-value=0.007). There was a moderate correlation between BPL and eGFR and a weak correlation between RCT and eGFR. Measuring BPL and RCT together correlated better with eGFR (R^2=0.181, p-value<0.001) compared with BPL (R^2=0.167, p-value<0.001) or RCT alone (R^2=0.073, p-value<0.01). It further found that, for sonographically determined BPL values below 8.6 cm or 6.9 cm, an adult CKD patient is likely to be in Stage 4 or Stage 5 disease, respectively. Similarly, an adult CKD patient is likely to be in Stage 4 or Stage 5 if the sonographically measured RCT is less than 4.8 mm or 1.3 mm, respectively.

Conclusions: Both BPL and RCT show a positive correlation with eGFR, however, BPL correlates better with eGFR than RCT among Ghanaian CKD patients. It also provided information on the values of BPL and RCT measurements for which adult CKD patients are likely to be in severe disease (that is CKD stages 4 and 5 or eGFR<30ml/min/1.73m2 and eGFR<15ml/min/1.73m2).

Keywords: Chronic kidney disease, estimated glomerular filtration rate, bipolar renal length, renal cortical thickness, ultrasound.

Background

The human kidney plays a vital role in acid-base and electrolyte balance, in addition to other synthetic and excretory functions [1]. Irreversibly damaged kidneys are unable to perform these functions [1]. Chronic kidney disease (CKD) refers to damaged kidneys with consequent abnormal excretion of albumin or impairment in renal function persisting for more than three months as evidenced by measured (mGFR) or estimated glomerular filtration rate (eGFR), the former being the gold standard [1].

Based on the GFR, CKD patients are classified into five main stages based on the KDIGO 2012 CKD Work Group guidelines [2].

The prevalence of CKD has risen in both developed and developing countries [3], with prevalence estimates of 13.3% and 8-10% for Ghana and Nigeria, respectively [4-6]. The disease demonstrates a slight male predominance in tropical Africa. The reported sex distribution among males and females in Ghana is 55% vs. 45%, respectively, attributable in part to higher risk factors of CKD such as hypertension and smoking among men and better health-seeking behaviour of females compared to males [7, 8].

In Africa, diabetes mellitus (DM), chronic hypertension, obesity, [3] chronic glomerulonephritis, human immunodeficiency virus (HIV) [7, 9], poverty and urbanization [10] are major contributors to the growing incidence of CKD.

Effective treatment regimens are required to prevent or delay the development of end-stage kidney disease [8]. Central to this goal is the monitoring of disease progression.

In clinical practice, ultrasound provides a useful technique for monitoring the progress of CKD and is preferred because of its simplicity, ease of use, cost-effectiveness, non-invasiveness, safety, ubiquity and wide accessibility, especially in resource-poor communities [11-14]. Ultrasound can aid in the diagnosis of some causes of CKD such as obstructive uropathy and predict irreversibility of renal damage, sparing patients unnecessary invasive and expensive diagnostic procedures [15].

Progressively, CKD results in the sequelae of shrunken/atrophic, sclerotic and fibrotic kidneys, with a decrease in renal bipolar length (BPL) [8, 16]. BPL measured with ultrasound has been shown to correlate positively with eGFR among CKD patients [17, 18], and has traditionally been the preferred, commonly reported sonographic parameter globally [13]. Recent studies have, however, reported a better correlation between renal cortical thickness (RCT) and eGFR [10, [12, 18, 19], citing a lag of the changes in BPL behind changes in RCT in some CKD etiological entities like DM, HIV, sickle cell and amyloid nephropathy. The confounding effects of body mass index (BMI), the Brenner rule of renal dosing and age on BPL arguably make RCT the preferred parameter in monitoring disease progression in CKD [12-15, 20, 21]. Proponents for the use of RCT believe that the location of glomeruli in the renal cortex means that its depletion in CKD affects RCT earlier than BPL [12, 15]. Unfortunately, literature on similar studies in sub-Saharan Africa is scanty or non-existent.

The increasing burden of CKD calls for concerted efforts to reduce the cost of patient monitoring and management [13]. Laboratory assays are adjunctive in tracking disease progression [14], but they are invasive, expensive and not widely available. Any attempt aimed at providing safe, readily available, cost-effective, and non-invasive means of evaluating patients with renal impairment and monitoring their renal function would be welcome news for clinicians and their CKD clients.

AIM AND OBJECTIVES

Aim

To determine the correlation between sonographically measured BPL and RCT with eGFR among adult CKD patients at a teaching hospital in Ghana.

Specific objectives

1. Estimate the mean renal bipolar length and mean renal cortical thickness of adult persons with established CKD using ultrasound.
2. Estimate the glomerular filtration rate (eGFR) of persons with established CKD using the MDRD formula.
3. Determine the correlation between sonographically measured mean renal bipolar length and mean renal cortical thickness at sonography and eGFR using statistical methods.
4. Determine the cut-off values of BPL and RCT measurements for which adult CKD patients are likely to be in severe disease.

METHODS

Study design and setting

A cross-sectional study was conducted at the out-patient clinic of the Renal and Dialysis Centre of the Department of Medicine and Therapeutics, Korle Bu Teaching Hospital (KBTH) between April and September 2021. The centre attends to both acute and chronic kidney disease patients. Ethical clearance was obtained from the KBTH Scientific and Technical Committee and Institutional Review Board.

Study population and sample size determination

The study population comprised CKD patients receiving treatment at the Renal and Dialysis Centre. The sample size was determined using the formula proposed by Charan and Biswas [22]. Using a prevalence rate of CKD of 13.3% for Ghana [6], a confidence level of 95%, and anticipated error margin of 5% to account for type 1 error, a 10% incremental adjustment was made to account for errors in administering questionnaires, resulting in the recruitment of 99 participants. Any consenting patient meeting the eligibility criteria was recruited.

Inclusion and exclusion criteria

All CKD outpatients ≥18years with a recent eGFR of not more than one (1) month were eligible for recruitment. CKD patients <18years, on dialysis, with hydronephrosis, renal cysts, echogenic kidneys that preclude optimal measurement of RCT, any other renal or abdominal lesions which could affect the accurate measurement of renal size were excluded from the study.

Data collection and procedures used

After obtaining voluntary informed consent, pre-tested questionnaires were administered to the patients to capture data on demographics, clinical history and co-morbidities like DM, hypertension, sickle cell disease, and HIV. Greyscale ultrasound scans of both kidneys were performed by a radiologist with experience in abdominal ultrasound. The radiologist was blinded to the patients' eGFR. All ultrasound scans were performed using the C-38 curvilinear array probe of a Toshiba Aplio 300 (Tokyo, Japan) with a probe frequency of 3.5 MHz in greyscale. RCT was measured in the sagittal plane at the mid-renal level. The RCT was taken over a medullary pyramid, perpendicular to the renal capsule as the longest distance from the renal capsule to the base of the medullary pyramid. The BPL was measured as the greatest pole-to-pole length in the longitudinal plane (Figure 1.0).

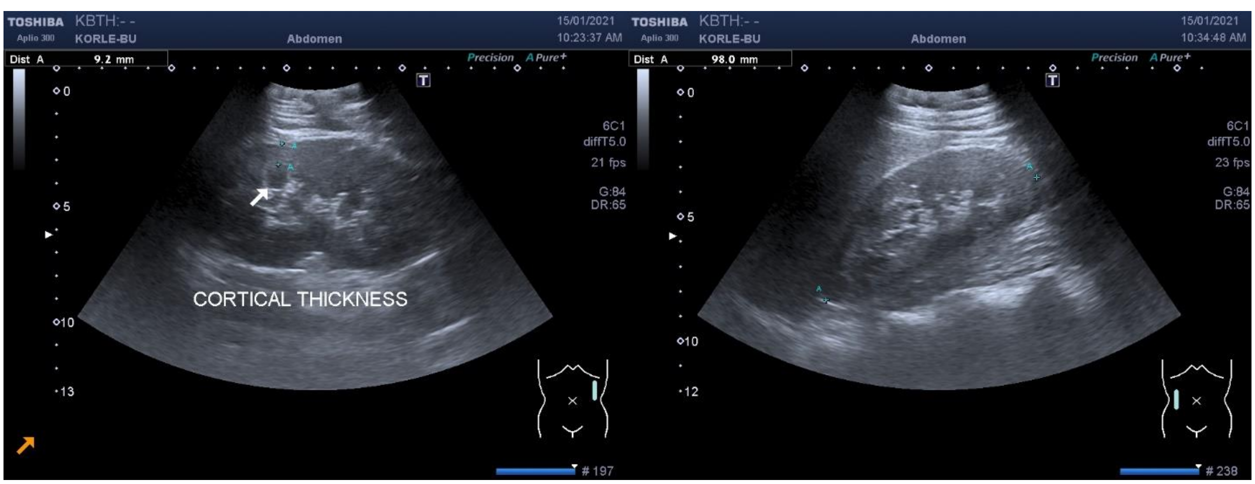

Figure 1.0 Longitudinal greyscale ultrasound showing A. measurement of left RCT over a renal pyramid (white arrow) denoted by callipers A-A and B. measurement of right BPL denoted by callipers A-A.

These measurements were done bilaterally. All measurements were taken in centimetres for BPL, and in millimetres for RCT, and recorded to one (1) decimal place. The mean BPL and mean RCT were then determined using the measurements on each kidney, also recorded to one (1) decimal place. All measurements were immediately recorded on data collection sheets. To ensure the accuracy of measurements, measurements for a sample of participants were taken 3 times and intra-rater reliability index was determined, with excellent reliability (>0.90). Body mass index was determined using a stadiometer.

The eGFR of patients were then computed and participants were grouped into various stages of CKD[2] using the most recent renal function/serum creatinine tests performed within the past one month and the results captured on data collection sheets. The eGFR was determined using the MDRD equation [23, 24] as follows:

$$\mathbf{eGFR=186.3\times SCr^{-1.154}\times Age^{-0.203}\times(0.742\ if\ female)\times(1.212\ if\ black),}$$ where SCr=serum creatinine.

Statistical Analysis

Data was analysed statistically with IBM Statistical Package for Social Sciences (SPSS) Version 23. Summary results of patients' characteristics were tabulated. Continuous data were analysed with descriptive statistics to generate means and standard deviations. Categorical variables are presented as counts and percentages. Spearman's rank correlation test and linear regression analysis were carried out to determine the correlation and strength of correlation, respectively, between eGFR, BPL and RCT, calculating for the coefficients of correlation (ρ) and determination (R^2). Spearman's rank correlation test was chosen because the data were non-parametric. The key dependent variable, eGFR, was not normally distributed (p-value=0.01) from the Shapiro-Wilk test of normality. Therefore, median as well as mean and range values were reported for eGFR. The statistical level of significance was set at a p-value<0.05.

RESULTS

Demographic characteristics of participants.

All 99 recruited participants completed the study. Of the 99 participants, there were 50.5% males (n=50) and 49.5% females (n=49). The mean age of the subjects was 55.6±12.4 (minimum=22, maximum=79) years. The age group with the least number of participants was 20-29 years (n=2, 2.0%); the age group with the highest number of participants was 50-59 years (n=29, 29.3%), Table 1.

Table 1 Sociodemographic characteristics of study participants

Age range (years)	n (%)
20-29	2.0 (2.0)
30-39	7.0 (7.1)
40-49	22.0 (22.2)
50-59	29.0 (29.3)
60-69	24.0 (24.2)
70-79	15.0 (15.2)

Key: n=number of participants; %=percentage

CLINICAL CHARACTERISTICS

eGFR and Stage of CKD

The mean eGFR for respondents was 42.8 mL/min/1.73m^2, (range of 2-547mL/min/1.73m^2.) The majority of respondents (n=40, 40.4%), had Stage 3 disease, with equal proportions of Stages 3a and 3b. This was followed by 22.2% (n=22) of respondents with Stage 5 disease as shown in Table 2.

Duration of sickness

The average duration of sickness since diagnosis was 2.2 years (range of 1 month to 8 years). The majority of respondents (n=43, 43.4 %) had been diagnosed with CKD for less than 1 year.

BMI

Of the study participants, 35.4% (n=35) had normal BMI (18.5 to 25); 4.0% (n=4) were underweight, 32.3% (n=32) were overweight and 28.3% (n=28) were obese.

Comorbidities

The commonest comorbid conditions of participants were chronic hypertension and DM. Of the number, 72 participants had hypertension (45 with hypertension only and 27 with both hypertension and DM), whilst 32 had DM (5 with DM only and 27 with both DM and hypertension] – as shown in Table 2.

Table 2 is a presentation of the clinical characteristics of the study participants.

Table 2. Clinical characteristics of participants.

Comorbidities	**n (%)**
HPTN	45.0 (45.5)
DM	5.0 (5.0)
Both HPTN and DM	27.0 (27.3)
SCDx	1.0 (1.0)
HIV	2.0 (2.0)
None	19.0 (19.2)
CKD Stage	**n (%)**
1	2.0 (2.0)
2	17.0 (17.1)
3A	20.0 (20.2)
3B	20.0 (20.2)
4	18.0 (18.2)
5	22.0 (22.2)

Key: n = number of participants; % =percentage; HPTN=Hypertension, DM=Diabetes mellitus, SCDx=Sickle cell disease, HIV=Human immunodeficiency virus, BMI=Body mass index.

Mean BPL and mean RCT

Table 3 is a summary of the mean BPL and RCT measured at ultrasound.

Table 3. Mean renal measurements at ultrasound

Variable	Mean BPL (cm) ±SD (range)	Mean RCT (mm) ±SD (range)
General	9.4±1.0 (7.0-12.0)	6.6±1.4 (2.8-10.9)
Right kidney	9.3±1.1 (7.1-12.0)	6.3±1.5 (2.8-10.4)
Left kidney	9.5±1.0 (7.0-12.0)	6.7±1.5 (3.7-10.9)
Males	9.4±1.0 (7.3-11.7)	6.5±1.5 (3.3-10.1)
Females	9.3±1.1 (7.0-12.0)	6.6±1.4 (3.5-10.1)

Key: SD= Standard deviation; BPL=Renal bipolar length; RCT=Renal cortical thickness.

The mean BPL was 9.4±1.0cm (minimum 7.0cm, maximum 12.0cm). On average, the kidneys measured 9.3±1.1cm and 9.5±1.0cm on the right and left, respectively. The mean BPL for males and females respectively were 9.4±1.0cm and 9.3±1.1cm. The mean RCT was 6.6±1.4mm (minimum 2.8mm, maximum 10.9mm). The mean RCT was 6.3±1.5mm and 6.7±1.5mm on the right and left, respectively. The mean RCT for males and females respectively were 6.5±1.5mm and 6.6±1.4mm.

BPL and RCT versus age

The mean BPL and RTC for various age groups are summarized in Table 4.

Table 4. Mean BPL, RCT and eGFR among various age groups

Age group (yrs.)	Mean BPL (cm) ±SD (range)	Mean RCT (mm) ±SD (range)	Mean eGFR (mL/min/1.73m^2) ±SD (range) [median]
<40	9.5±0.6 (8.6-12.0)	6.8±2.3 (3.4-9.2)	46.2±27.2 (11.0-146.0) [42.5]
40-49	9.4±1.2 (7.8-11.8)	6.5±1.7 (3.5-10.1)	34.1±23.6 (2.0-78.0) [29.5]
50-59	9.2±1.0 (7.3-10.8)	6.4±1.2 (4.1-9.2)	46.7±98.0 (6.0-547.0) [24.0]
60-69	9.6±0.9 (8.2-11.5)	6.6±1.4 (4.6-10.1)	41.4±21.3 (6.0-76.0) [43.0]
70-79	9.2±1.0 (7.0-10.5)	6.3±1.3 (3.5-8.3)	41.3±21.0 (9.0-72.0) [39.0]
Mean(total)	9.4±1.0 (7.0-12.0)	6.6±1.4 (3.4-10.1)	42.8±56.7 (2-547.0) [37.0]

Key: yrs.=years; SD=standard deviation; BPL=Renal bipolar length; RCT=Renal cortical thickness; eGFR=estimated glomerular filtration rate.

The smallest BPL was recorded among the 50-59 year and 70-79 year age groups whiles the largest BPL was recorded among the 60-69 year age group. Similarly, the smallest and largest mean RCT was recorded among age groups 70-79 years and <40 years, respectively.

BPL and RCT versus duration since diagnosis

Table 5 is a summary of the various sonographic measurements for different durations of CKD since diagnosis.

Table 5. Mean BPL, RCT and eGFR for various sickness since diagnosis

Duration (yrs.)	**Mean BPL (cm) ±SD (range)**	**Mean RCT (mm) ±SD (range)**	**Mean eGFR (mL/min/1.73m^2) ±SD (range) [median]**
<1	9.6±1.0 (7.8-12.0)	6.6±1.5 (3.3-9.2)	41.3±27.1 (2.0-146.0) [37.0]
1	9.4±0.5 (8.6-9.9)	6.6±1.1 (5.3-8.3)	29.4±18.6 (8.0-58.0) [23.0]
2	9.1±0.9 (7.3-10.2)	6.6±1.3 (4.7-9.2)	79.7±156.3 (7.0-547.0) [39.0]
3	9.3±1.2 (7.7-11.8)	6.3±1.7 (3.7-10.1)	37.8±29.0 (5.0-79.0) [36.0]
4	8.8±1.1 (7.0-10.3)	6.9±1.6 (5.5-10.1)	39.6±21.4 (10.0-68.0) [42.0]
5	8.2±0.3 (7.9-8.4)	5.9±2.9 (3.9-8.0)	23.0±2.8 (21.0-25.0) [23.0]
6	9.1±1.1 (7.3-10.5)	5.6±1.1 (3.5-7.1)	23.9±17.6 (6.0-58.0) [22.0]
7	9.0±1.0 (7.8-9.8)	7.1±1.7 (5.3-8.7)	38.7±20.0 (18.0-58.0) [40.0]
8	10.1±1.7 (8.9-11.3)	6.8±0.1 (6.7-6.9)	64.0±19.8 (50.0-78.0) [64.0]

Key: yrs.=years; SD=standard deviation; BPL=Renal bipolar length; RCT=Renal cortical thickness; eGFR=estimated glomerular filtration rate.

Patients who had been diagnosed with CKD for 5 and 8 years, respectively had the smallest and largest mean BPL values. Mean RTC was smallest among patients with an average duration of sickness of 5 years and largest among those with an average duration of sickness of 7 years.

BPL and RCT versus comorbidities.

The various comorbidities with their mean BPL and RCT are summarized in Table 6.

Table 6. Mean BPL, RCT and eGFR for various comorbidities

Comorbidities	**Mean BPL (cm) ±SD (range)**	**Mean RCT (mm) ±SD (range)**	**Mean eGFR (mL/min/1.73m^2) ±SD (range) [median]**
HPTN	9.2±1.1 (7.3-11.8)	6.5±1.3 (3.5-9.2)	27.4±20.9 (2.0-79.0) [19.0]
DM only	9.8±0.9 (9.2-10.8)	7.2±1.7 (5.5-8.9)	34.3±4.0 (30.0-38.0) [35.0]
SCDx	9.4±0.8 (7.0-10.8)	6.8±1.3 (3.5-10.1)	62.4±98.3 (8.0-547.0) [45.0]

Key: SD=standard deviation, BPL=Renal bipolar length; RCT=Renal cortical thickness; eGFR=estimated glomerular filtration rate.

Amongst patients with comorbidities, both mean BPL and RCT were smallest for those with hypertension and largest for those with DM, followed by SCDx.

BPL and RCT versus BMI

The mean BPL and RCT for various BMI groups are presented in Table 7.

Table 7. Mean BPL, RCT and eGFR for various BMIs

BMI	**Mean BPL (cm) ±SD (range)**	**Mean RCT (mm) ±SD (range)**	**Mean eGFR (mL/min/1.73m^2) ±SD (range) [median]**
<18.5	9.4±0.9 (8.6-10.5)	6.3±0.5 (5.6-6.8)	63.3±15.9 (41.0-77.0) [67.0]
18.5-24.9	9.1±1.2 (7.0-12.0)	6.1±1.6 (3.3-10.1)	30.9±21.1 (2.0-82.0) [44.5]
25-29.9	9.5±0.9 (7.8-11.5)	6.6±1.2 (3.5-9.2)	49.5±92.0 (6.0-547.0) [33.0]
≥30	9.5±0.9 (7.8-11.8)	7.0±1.5 (3.5-10.1)	44.9±27.1 (5.0-146.0) [36.0]

Key: SD=standard deviation; BPL=Renal bipolar length; RCT=Renal cortical thickness; eGFR=estimated glomerular filtration rate.

Mean BPL was smallest among patients with normal BMI, and largest among overweight and obese patients. Mean RCT was largest among obese patients and smallest for patients with normal BMI.

Figure 2.0 is a representative greyscale ultrasound image of a 73 year-old female hypertensive, diagnosed with CKD about 5 years prior and current serum creatinine of 461.2 µmol/L, eGFR of 8 mls/min/1.73m^2 showing decreased BPL of 7.5 cm and decreased RCT of 6.5 mm.

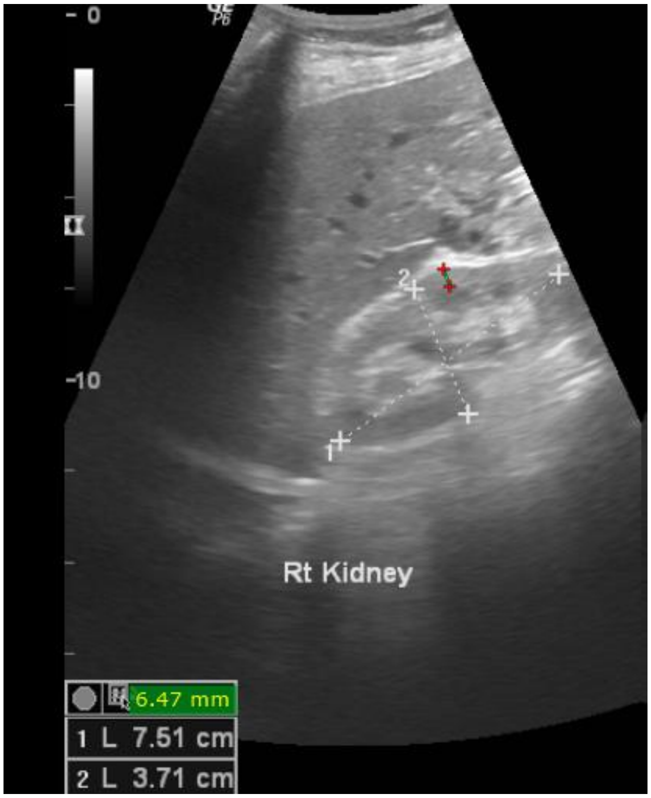

Figure 2: Greyscale ultrasound scan of the right kidney of a 73 year-old, female hypertensive and CKD patient showing BPL (white callipers 1) and RCT (red callipers).

INFERENTIAL STATISTICS

Correlation between measured ultrasound and clinical parameters of CKD patients

The correlation between the sonographic and clinical parameters of the CKD patients was tested with Spearman's correlation coefficient (ρ). The coefficient of determination (R^2) was evaluated using linear regression analysis to test for the strength of correlation.

The coefficients of correlation (ρ) of mean BPL and RCT with age and eGFR, with their tests of statistical significance are summarized in Table 8.0 below. Figures 3.0 and 4.0 are scatter plots with lines of best fit of eGFR against BPL and RCT.

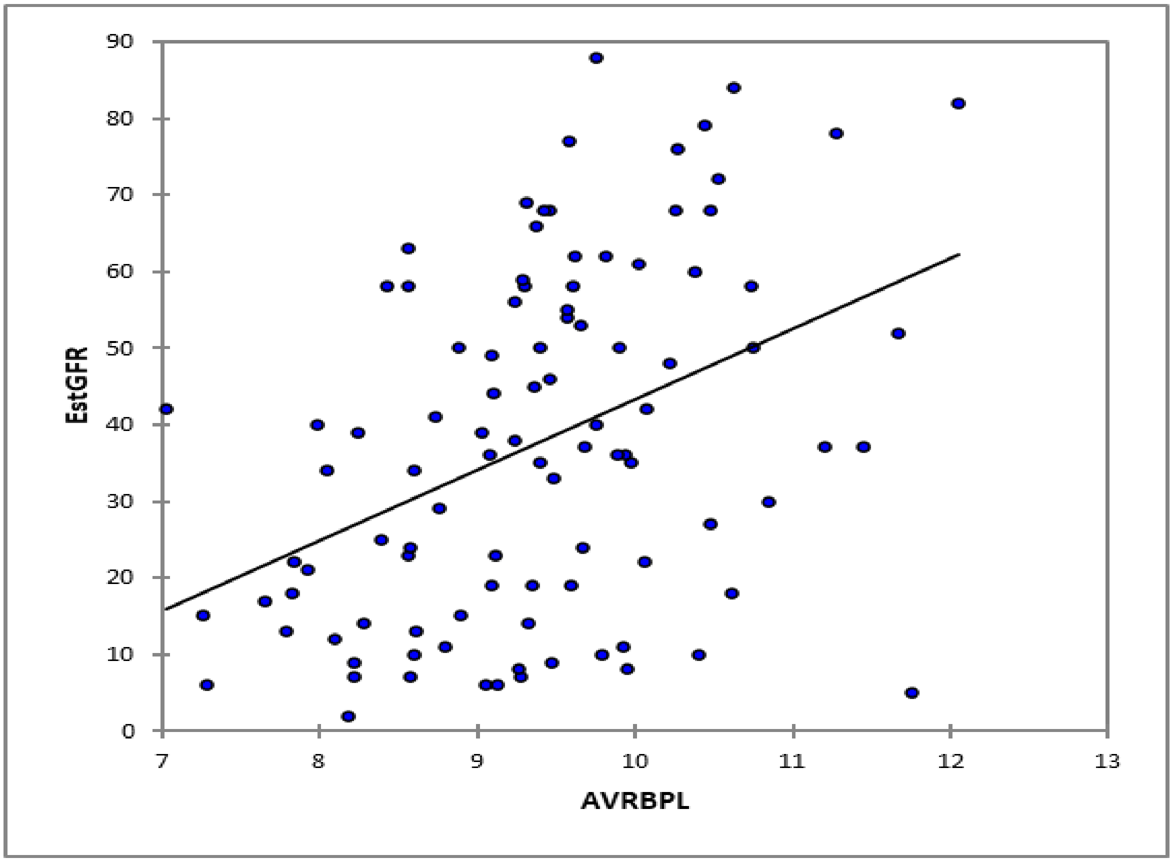

Figure 3.0 Scatter plot of eGFR against BPL with line of best fit

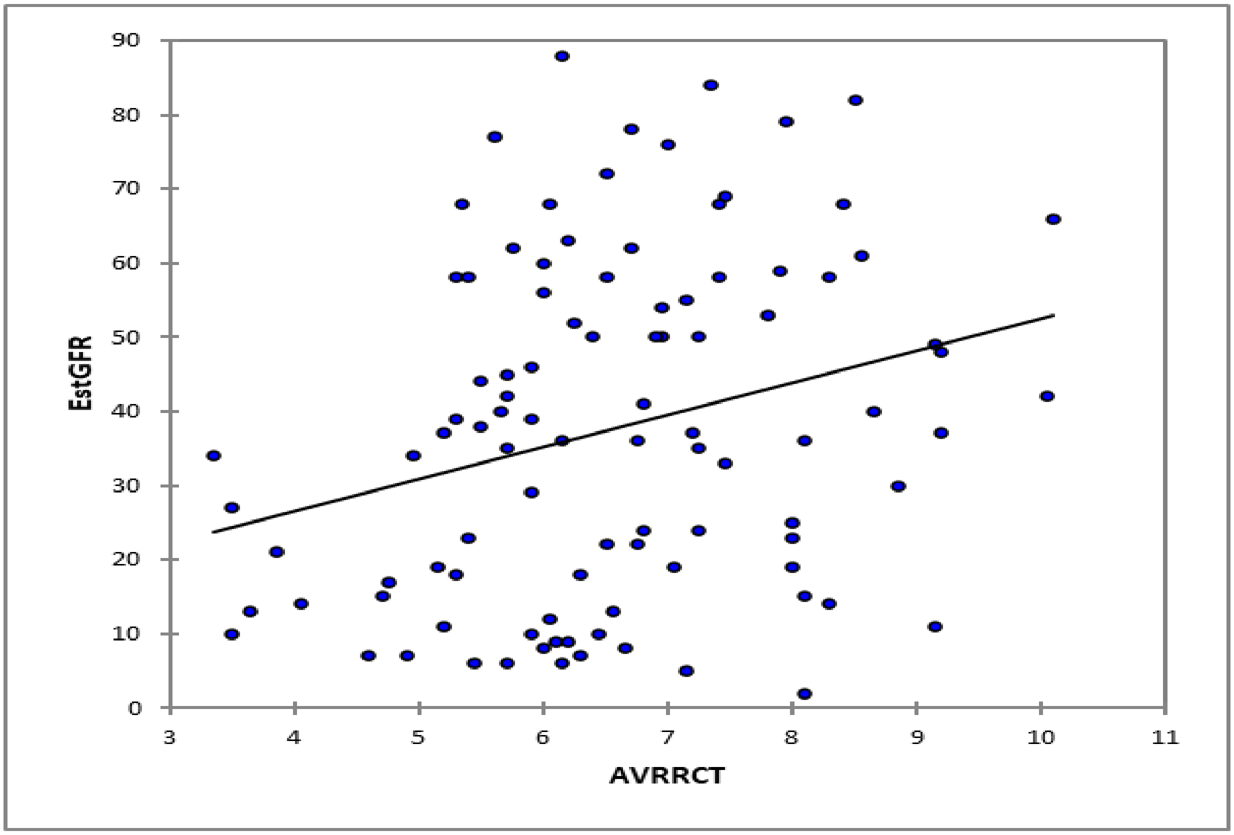

Figure 4.0 Scatter plot of eGFR against RCT with line of best fit

Table 8.0 Spearman's coefficient of correlation between BPL/RCT and age/eGFR.

Variable	P	**p-value**
Mean BPL vs. Age	-0.045	0.656
Mean BPL vs. eGFR	0.406	<0.001*
Mean RCT vs. Age	-0.165	0.103
Mean RCT vs. eGFR	0.270	0.007*

Key: *=Statistically significant; ρ=Spearman's coefficient of correlation; BPL=Renal bipolar length; RCT=Renal cortical thickness; eGFR=estimated glomerular filtration rate.

Correlation of mean BPL with age and eGFR

From Table 8.0, mean BPL showed a negative correlation with age (ρ= -0.045, p-value=0.656). That is, increasing age corresponded with a decline in mean BPL. The correlation, however, was not statistically significant (p-value>0.05). There was a statistically significant positive correlation (p-value<0.05) between eGFR and mean BPL (ρ=0.406, p-value < 0.001).

Correlation of mean RCT with age and eGFR

From Table 8.0, the mean RCT declined as age (ρ= -0.165, p-value=0.103) increased. The correlation, however, was not statistically significant (p-value>0.05). There was a statistically significant positive correlation of mean RCT with eGFR (ρ=0.270, p-value=0.007).

Strength of correlation between mean BPL, RCT and eGFR

Linear regression analysis was done to determine the strength/significance of correlation of eGFR with BPL and RCT. The coefficients of determination (R^2) of eGFR with mean BPL and RCT were calculated. Both mean BPL and RCT showed statistically significant correlations with eGFR (p-value<0.05). However, there was stronger correlation between eGFR and mean BPL, with a moderate coefficient of determination (ρ=0.406, R^2=0.167). Comparatively, the correlation between mean RCT and eGFR was weaker, (ρ=0.270, R^2=0.073).

Strength of correlation between a combination of mean BPL and RCT against eGFR

Multiple linear regression analysis was done (Table 9.0) to assess how measuring mean BPL and RCT together influences eGFR. Mean BPL and RCT, when taken together, improved the strength of correlation with eGFR (R^2=0.181, p-value<0.05). However, the effect of mean RCT was very insignificant (p-value=0.203) compared with mean BPL (p-value=0.001).

Table 9.0 Multiple linear regression of combination of BPL and RCT with eGFR

Model	**Unstandardized Coefficients**		**Standardized Coefficients**	**t**	**Sig.**	**R^2**	**Adjusted R^2**
	B	Std. Error	Beta				
(Constant)	-51.760	19.818		-2.612	.010	0.181	0.164
Mean RCT	2.064	1.608	.129	1.283	.203		
Mean BPL	.809	.228	.357	3.554	.001		

Cut off values of BPL and RCT for severe CKD

Simple linear regression analysis was done (Tables 10 and 11) to determine the values of BPL and RCT measurements for which adult CKD patients are likely to be in severe disease (that is CKD stages 4 and 5 or eGFR<30ml/min/1.73m^2 and eGFR<15ml/min/1.73m^2). The cut-off values for Stage 4 CKD were calculated to be 8.6 cm for BPL and 4.8 mm for RCT, while those for Stage 5

CKD/ESRD were 6.9 cm for BPL and 1.3 mm for RCT. In other words, for sonographically determined BPL values below 8.6 cm or 6.9 cm, an adult CKD patient is likely to be in Stage 4 or Stage 5 disease, respectively. Similarly, an adult CKD patient is likely to be in Stage 4 or Stage 5 if the sonographically measured RCT is less than 4.8 mm or 1.3 mm, respectively. Both cut-off values were statistically significant (p-value <0.0001 with 95% CI of 5.08 – 13.40 for BPL; and p-value =0.007 with 95% CI of 1.22 – 7.43 for RCT).

Table 10: Simple linear regression of BPL with eGFR

Source	Value	Standard error	t	Pr > |t|	Lower bound (95%)	Upper bound (95%)
(Constant)	-49.0653	19.7721	-2.4815	0.0148	-88.3074	-9.8233
BPL	9.2410	2.0966	4.4076	< 0.0001	5.0798	13.4022

Table 11: Simple linear regression of RCT with eGFR

Source	Value	Standard error	t	Pr > |t|	Lower bound (95%)	Upper bound (95%)
(Constant)	9.2499	10.4809	0.8825	0.3797	-11.5518	30.0516
RCT	4.3244	1.5632	2.7663	0.0068	1.2219	7.4270

DISCUSSION

The study showed a slight male predominance of CKD, which agrees with other studies done in Ghana and other African populations [7, 25]. Additionally, more males (13.1%) had end-stage/Stage 5 disease compared to females (9.1%). Several studies postulate that the male gender tends to be more predisposed to CKD and its rapid progression to end-stage disease [26] while the female gender is protective [27]. This is because there is a male preponderance in significant risk factors of renal disease like hypertension and diabetes mellitus [7, 8, 25]. Again, females tend to have better health-seeking behaviour than males [7, 8, 25].

The mean age for study participants was 55.6±12.4years, similar to findings from other studies among CKD patients in the sub-region [5, 8]. This mean age also coincides with a mean age of 55 years for chronic hypertension in Africa [28] and may be explained by the fact that hypertension is the leading cause of CKD in Africa [5]. Age has been shown to be an independent predictor of CKD [29]. GFR is estimated to decline by 0.75ml/min/year in normal individuals beyond 30 years, as a result of decreasing renal mass and increasing glomerular sclerosis with age [29]. This physiological decline in renal function with age can be further worsened by conditions like DM and hypertension, making CKD more prevalent among ageing people [29].

Most (72.8%) of the study participants had hypertension, whilst 32.3% had DM – alone or as a combination – both of which are consistent with previous studies conducted in Ghana [27, 30]. Hypertension [5, 31] and DM [8] respectively are the commonest and second most common causes of CKD in Africa [5, 8, 31] in keeping with the two conditions being the top two comorbidities among CKD patients in this study.

The difference between the mean right and left BPL was 5.0mm, the left being slightly larger than the right consistent with findings from a study by Moghazi et al [32], who found a mean difference of 7.0mm between the smaller right and the larger left renal lengths. The mean BPL for males and females respectively were 9.4±1.0cm and 9.3±1.1cm, with no significant difference between this dimension for the two sexes. Studies elsewhere have supported this finding [13].

The mean BPL and RCT were 9.4±1.0cm and 6.6±1.4mm, respectively. Similar findings were made from similar studies conducted among CKD patients in Africa, Asia, North and South America [10, 12, 19]. Compared with the mean BPL among normal subjects [33], the BPL among the CKD study subjects had shrunk by 1.8 cm on the left and 1.5 cm on the right, consistent with the pathophysiology of CKD. Though age showed a negative correlation with BPL (and RCT), the relationship was not statistically significant (p-value=0.656), and hence this decline in BPL is largely attributable to CKD. BMI also showed a positive but statistically insignificant correlation with BPL (p-value=0.168).

Both mean BPL and RCT showed a statistically significant correlation with eGFR, which agrees with findings by Korkmaz et al [10] and Adibi et al [33]. This index study, however, shows that, of the two parameters, BPL had a stronger correlation with the eGFR/CKD stage than RCT. Again, there was an improvement in the strength of correlation with eGFR when the two sonographic parameters were measured together (R^2=0.181, p-value<0.05) compared with either mean BPL alone (R^2=0.167, p-value<0.001) or RCT alone (R^2=0.073, p-value<0.01). However, of the two, the effect of mean RCT was insignificant (p-value=0.203) compared with mean BPL (p-value=0.001). This contrasts with the findings by Korkmaz et al [10], Yamashita et al [12], and Beland et al [19], who found a stronger correlation between RCT and eGFR than BPL and eGFR. The difference could be accounted for by the fact that, compared with the Ghanaian population where the commonest comorbid condition is hypertension, the commonest cause of CKD in developed countries is DM [34]. Some researchers believe that the decrease in renal length in DM lags behind RCT as CKD progresses [12]. It is therefore not surprising that in jurisdictions with high DM, unlike Ghana, RCT correlates better with eGFR than BPL. When the data were further explored to determine the cut-off values of BPL and RCT measurements for which adult CKD patients are likely to be in severe disease, the findings showed that for sonographically determined BPL values below 8.6 cm or 6.9 cm, an adult CKD patient is likely to be in Stage 4 or Stage 5 disease, respectively. Similarly, an adult CKD patient is likely to be in Stage 4 or Stage 5 if the sonographically measured RCT is less than 4.8 mm or 1.3 mm, respectively. Since both cut-off values were statistically significant, these present novel findings which can have clinical implications.

As has been demonstrated in the index study and other studies, hypertension is the most common cause of CKD among Ghanaians [30]. The effects of hypertension on the kidneys include benign and malignant nephrosclerosis and accelerated glomerulosclerosis, resulting in a reduction in renal size. This makes renal size a good predictor of worsening renal function. This is corroborated by a study which compared sonographically measured renal parameters with underlying histologically confirmed causes of CKD [32]. Comparing the effect of sclerosed glomeruli, interstitial fibrosis and tubular atrophy on renal length and cortical thickness, the study [32] showed that renal length demonstrated a statistically significant correlation with renal function for all the identified histopathologic causes of CKD, relative to cortical thickness for the same histopathologic findings [32]. Though this index study did not include the histologic diagnosis underlying the renal impairment of study participants, it confirms the suggestion that BPL may be a better predictor of renal impairment than RCT, especially in areas with hypertension as the major cause of CKD. A study in Nigeria to confirm the pathologic basis of end-stage renal disease demonstrated that 43% of CKD cases were due to hypertensive nephrosclerosis [5] also supporting the finding of hypertension being the commonest comorbid disease in this study. Consequently, BPL would be expected to correlate better with worsening eGFR, relative to RCT.

Though age has been shown to affect BPL and RCT [12, 33], and the findings from this study showed a somewhat progressive decline in BPL and RCT with age (Table 4), the correlation between age and the two parameters was not statistically significant. Age does not play a significant role in the decline of BPL and RCT among CKD patients.

Conclusions

The study has shown that amongst Ghanaian CKD patients, eGFR shows a statistically significant correlation with BPL and RCT, the former having a stronger correlation. This study shows that eGFR, BPL and RCT can be used together for comprehensive management of CKD patients. It also provided information on the values of BPL and RCT measurements for which adult CKD patients are likely to be a severe disease (that is CKD stages 4 and 5 or eGFR<30ml/min/1.73m2 and eGFR<15ml/min/1.73m2). Specifically, it demonstrated that for sonographically determined BPL values below 8.6 cm or 6.9 cm, an adult CKD patient is likely to be in Stage 4 or Stage 5 disease, respectively. Similarly, an adult CKD patient is likely to be in Stage 4 or Stage 5 if the sonographically measured RCT is less than 4.8 mm or 1.3 mm, respectively.

RECOMMENDATIONS

It is recommended that further multicentre studies with larger numbers and non-CKD control subjects be conducted to validate or otherwise, the findings of this study. The health authorities in Ghana and the scientific community should come together to establish normative sonographic reference values for the Ghanaian population and possibly find the critical values for BPL and RCT beyond which any size reduction could be attributable to CKD.

Finally, a study comparing the effect of the various histological diagnoses of CKD on BPL and RCT will also help with better management and follow-up of CKD patients.

LIMITATIONS OF STUDY

The use of eGFR instead of 24-hour creatinine clearance which is a better predictor of renal impairment is a major limitation in assessing renal function of the patients.

The study did not recruit normal subjects as controls due to the cost implications of paying for normal patients to have renal function assessment and ultrasound of the kidney. The use of controls would have provided a better form of validation for the findings of this study. A small sample size of 99 patients was used, due to time and resource constraints. Future studies with larger numbers are recommended.

List of abbreviations

BMI –	Body mass index
BPL –	Bipolar length
CG –	Cockcroft-Gault
CKD –	Chronic kidney disease
CT –	Computed tomography
DM –	Diabetes mellitus
eGFR –	Estimated glomerular filtration rate
HIV –	Human immunodeficiency virus
IVC –	Inferior vena cava
KBTH –	Korle Bu Teaching Hospital
MDRD –	Modification of diet in renal disease
MRI –	Magnetic resonance imaging
RCT –	Renal cortical thickness
RRT –	Renal replacement therapy
USG –	Ultrasonography

REFERENCES

1. K/DOQI. Clinical practice guidelines for chronic kidney disease: evaluation, classification and stratification. Am J Kidney Dis. 2002 Feb;39(2 Suppl 1):S1–266.

2. Kidney Disease: Improving Global Outcomes (KDIGO) CKD Work Group. KDIGO 2012 Clinical Practice Guideline for the Evaluation and Management of Chronic Kidney Disease. Kidney Int Suppl. 2013. 3:1-150.

3 Sumaili EK, Krzesinski JM, Zinga CV, Cohen EP, Delanaye P, Munyanga SM, et al. Prevalence of chronic kidney disease in Kinshasa: results of a pilot study from the Democratic Republic of Congo. Nephrol Dial Transplant. 2009 Jan;24(1):117-22. doi: 10.1093/ndt/gfn469.

4. Akinsola W, Odesanmi WO, Ogunniyi JO, Ladipo GO. Diseases causing chronic renal failure in Nigerians - a prospective study of 100 cases. Afr J Med Med Sci. 1989 Jun;18(2):131–7.

5. Ojo OS, Akinsola AA, Nwosu SO, Odesanmi WO. The pathological basis of chronic renal failure in Nigerians; an autopsy study. Trop Geogr Med. 1992 Jan;44(1-2):42–6.

6. Adjei DN, Stronks K, Adu D, Beune E, Meeks K, Smeeth L, et al. Chronic kidney disease burden among African migrants in three European countries and in urban and rural Ghana: the RODAM cross-sectional study. Nephrol Dial Transplant. 2018 Oct 1;33(10):1812-1822. doi: 10.1093/ndt/gfx347.

7. Eghan BA, Amoako-Atta K, Kankam CA, Nsiah-Asare A. Survival pattern of hemodialysis patients in Kumasi, Ghana: a summary of forty patients initiated on hemodialysis at a new hemodialysis unit. Hemodial Int. 2009 Oct;13(4):467–71.

8. Ampem Amoako Y, Laryea DO, Bedu-Addo G, Andoh H, Asante Awuku Y. Clinical and demographic characteristics of chronic kidney disease patients in a tertiary facility in Ghana. The Pan African Medical Journal. 2014;18:274. doi:10.11604/pamj.2014.18.274.4192

9. de-Graft Aikins A, Unwin N, Agyemang C, Allotey P, Campbell C, Arhinful D. Tackling Africa's chronic disease burden: from the local to the global. Global Health. 2010 Apr 19;6:5. doi: 10.1186/1744-8603-6-5.

10. Korkmaz M, Aras B, Güneyli S, Yılmaz M. Clinical significance of renal cortical thickness in patients with chronic kidney disease. Ultrasonography. 2018 Jan;37(1):50-54. doi: 10.14366/usg.17012.

11. Ninan VT, Koshi KT, Niyamthullah MM, Jacob CK, Gopalakrishnan G, Pandey AP, et al. A comparative study of methods of estimating renal size in normal adults. Nephrol Dial Transplant. 1990;5(10):851-4. doi: 10.1093/ndt/5.10.851.

12. Yamashita SR, von Atzingen AC, Iared W, Bezerra AS, Ammirati AL, Canziani ME, et al. Value of renal cortical thickness as a predictor of renal function impairment in chronic renal disease patients. Radiol Bras. 2015;48(1):12-6. doi: 10.1590/0100-3984.2014.0008.

13. El-Reshaid W, Abdul-Fattah H. Sonographic assessment of renal size in healthy adults. Med Princ Pract. 2014;23:432–436.

14. O'Neill WC. Sonographic evaluation of renal failure. Am J Kidney Dis. 2000 Jun;35(6):1021-38. doi: 10.1016/s0272-6386(00)70036-9.

15. Buturovic-Ponikvar J, Visnar-Perovic A. Ultrasonography in chronic renal failure. Eur J Radiol. 2003;46:115–122.

16. Lederer E, Ouseph R. Chronic kidney disease. Am J Kidney Dis. 2007;49:162-171.

17. Ozmen CA, Akin D, Bilek SU, Bayrak AH, Senturk S, Nazaroglu H. Ultrasound as a diagnostic tool to differentiate acute from chronic renal failure. Clin Nephrol. 2010 Jul;74(1):46-52.

18. Van Den Noortgate N, Velghe A, Petrovic M, Vandewiele C, Lameire N, Voet D, et al. The role of ultrasonography in the assessment of renal function in the elderly. J Nephrol. 2003;16:658-662.

19. Beland MD, Walle NL, Machan JT, Cronan JJ. Renal cortical thickness measured at ultrasound: is it better than renal length as an indicator of renal function in chronic kidney disease? AJR Am J Roentgenol. 2010 Aug;195(2):W146-9. doi: 10.2214/AJR.09.4104.

20. Buchholz NP, Abbas F, Biyabani SR, Afzal M, Javed Q, Rizvi I, et al. Ultrasonographic renal size in individuals without known renal disease. J Pak Med Assoc. 2000 Jan;50(1):12-16.

21. Otiv A, Mehta K, Ali U, Nadkarni M. Sonographic measurement of renal size in normal Indian children. Indian Pediatr. 2012 Jul;49(7):533-6. doi: 10.1007/s13312-012-0120-7.

22. Charan J, Biswas T. How to calculate sample size for different study designs in medical research?. Indian J Psychol Med. 2013;35(2):121–126. doi:10.4103/0253-7176.116232.

23. Levey AS, Coresh J, Greene T, Stevens LA, Zhang YL, Hendriksen S, et al. Using standardized serum creatinine values in the modification of diet in renal disease study equation for estimating glomerular filtration rate. Ann Intern Med. 2006;145:247-254.

24. Levey AS, Greene T, Kusek SW, Beck GJ. A simplified equation to predict glomerular filtration rate from serum creatinine. J Ann Soc Nephrol. 2000;11:155A.

25. Ulasi II, Ijoma CK. The enormity of chronic kidney disease in Nigeria: the situation in a Teaching Hospital in South - East Nigeria. J Trop Med. 2010 Jun;2010:501957.

26. Neugarten J, Acharya A, Silbiger SR. Effect of gender on the progression of nondiabetic renal disease: a meta-analysis. J Am Soc Nephrol. 2000;11(2):319-329.

27. Tannor EK, Sarfo FS, Mobula LM, Sarfo-Kantanka O, Adu-Gyamfi R, Plange-Rhule J. Prevalence and predictors of chronic kidney disease among Ghanaian patients with hypertension and diabetes mellitus: A multicenter cross-sectional study. J Clin Hypertens (Greenwich). 2019 Oct;21(10):1542-1550. doi: 10.1111/jch.13672.

28. Kaze AD, Schutte AE, Erqou S, Kengne AP, Echouffo-Tcheugui JB. Prevalence of hypertension in older people in Africa: a systematic review and meta-analysis. J Hypertens. 2017;35(7):1345-52.

29. Coresh J, Astor BC, Greene T, Eknoyan G, Levey AS. Prevalence of chronic kidney disease and decreased kidney function in the adult US population: third National Health and Nutrition Examination Survey. Am J Kidney Dis. 2003;41(1):1-12.

30. Osafo C, Mate-Kole M, Affram K, Adu D. Prevalence of chronic kidney disease in hypertensive patients in Ghana. Ren Fail. 2011;33(4):388-392.

31. Arogundade FA, Barsoum RS. CKD prevention in Sub-Saharan Africa: a call for governmental, nongovernmental, and community support. Am J Kidney Dis. 2008;51(3):515-523.

32. Moghazi S, Jones E, Schroepple J, Arya K, McClellan W, Hennigar RA, et al. Correlation of renal histopathology with sonographic findings. Kidney Int. 2005;67:1515–1520.

33. Emamian SA, Nielsen MB, Pedersen JF, Ytte L. Kidney dimensions at sonography: correlation with age, sex, and habitus in 665 adult volunteers. AJR Am J Roentgenol. 1993 Jan;160(1):83-6. doi: 10.2214/ajr.160.1.8416654.

34. Coresh J, Selvin E, Stevens LA, Manzi J, Kusek JW, Eggers P, et al. Prevalence of chronic kidney disease in the United States. JAMA. 2007 Nov 7;298(17):2038-47. doi: 10.1001/jama.298.17.2038.