Ultrasound Correlation of Renal indices with Creatinine levels in Chronic Kidney Disease In a tertiary hospital, South south Nigeria: A pilot study,

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Introduction

Chronic kidney disease (CKD) is characterized by a gradual decline in renal function, as indicated by a glomerular filtration rate of 60 mL/min/1.73 m2 or impaired kidney function lasting for a minimum of 3 months1. Chronic kidney disease (CKD) is characterized by the loss of more than 50% of nephrons, resulting in impaired excretory function and an elevated risk of cardiovascular complications 2,3. Serum creatinine is naturally produced and filtered by healthy kidneys, but it builds up when kidney function is decreased, which helps determine the stage of chronic kidney disease (CKD).3 The global prevalence of CKD varies between 8-19.9%, with a range of which is influenced by different definitions and populations 4-5. The frequency in Nigeria varies between 8% and 45.5%, contingent upon the specific context and presence of comorbidities6-7. Chronic kidney disease (CKD) exhibits a higher prevalence among young adults in sub-Saharan Africa compared to affluent nations, mostly due to the presence of endemic infections and the increasing prevalence of non-communicable diseases. such as glomerulonephritis, HIV and increasing incidence of essential hypertension and diabetes 11,12 The individual and economic burden is substantial as a result of the expenses associated with treatment and the restricted availability of renal replacement therapy13-16. The importance of early detection and prevention cannot be overstated 17.

Chronic kidney disease (CKD) diagnosis combines clinical characteristics with blood and urine biomarkers and imaging techniques1. Renal ultrasonography is a non-invasive method that examines the structure of the kidneys without the use of radiation, and it can help uncover treatable problems18,-21. Advanced disease is shown by the presence of small, echogenic kidneys.20

The aim of this study was to investigate the potential correlation between renal length, cortical echogenicity, and corticomedullary differentiation on ultrasonography and serum creatinine levels in patients with chronic kidney disease (CKD) in Nigeria. These correlations have the potential to facilitate the use of ultrasonography in estimating glomerular filtration rates, hence assisting in the diagnosis and monitoring of low-access laboratories. Establishing connections between imaging and biomarkers could enhance the characterization of chronic kidney disease (CKD) in areas with limited resources.

**Study Design and Setting**

This cross-sectional study was conducted over 12 months at the radiology department in the University of Port Harcourt Teaching Hospital, a tertiary hospital in Port Harcourt, Nigeria. Adult CKD patients aged 18-65 years referred from the nephrology unit were recruited. CKD was defined1 as evidence of kidney damage ± glomerular filtration rate <60 mL/min/1.73m2.Sample Size was calculated using Fisher's formula21 and 10% CKD prevalence from a prior study,22 150 patients were enrolled into the study. Serum creatinine analysis using a modified Jaffe kinetic method was done. Ethical approval23 was obtained from the Hospital Ethics Committee. Bivariate correlations between continuous variables were assessed using Spearman’s rank correlation coefficient due to non-normal distributions. Multivariable linear regression with creatinine as the dependent variable was performed using stepwise selection of independent predictors with p<0.05 for entry and retention in the model

**Inclusion criterion**

Patients diagnosed with CKD in the Nephrology Unit (as evidenced by presence of markers of chronic kidney damage whether or not the GFR is reduced) and patients with CKD who were between the ages of 18years and 65years (young and middle aged adults) .

**Exclusion criteria**

Patients who had any form of renal replacement therapy (dialysis or renal transplant), patients with fatty liver 24 (because their liver echoes will be raised, thus making it difficult to detect increased renal cortical echogenicity in early stages of CKD) or pregnant women (as physiological renal changes in pregnancy may mask CKD).

**Imaging protocol and Analysis**

Ultrasounds were performed using a. Mindray DC-6 ultrasound machine with a 2.5-3.5 MHz convex probe for all ultrasound exams. The tests were conducted under supervision of by two experienced radiologists. Various imaging techniques like speckle reduction imaging and low tissue harmonic imaging were used to improve the visualization of organ echogenicity. The gain and time gain compensation adjustments were made manually for each patient to ensure impartiality thus adjusting the image quality as needed. Furthermore, information on the serum creatinine level of each patient during the scans was blind to the sonologist. Differences in the observations were re-evaluated till a consensus was reached.

The following parameters were measured (Figure 1):

1. Renal length: Longitudinal bipolar maximum (pole to pole)-normal length :9-12cm
2. Cortico-medullary differentiation was assessed as visualization of the pyramid /cortex as being distinct from the sinus and graded as being maintained, poorly maintained or lost.
3. Cortical echogenicity: Graded 0-4 vs. liver echogenicity and differentiation.

Renal Cortical Echogenicity Grading25

Renal cortical echogenicity was graded on a scale of 0-4 by comparing it to the echogenicity of the liver and medulla, using a standardized grading scale to the liver :

1. Less echogenic than the liver
2. Equal echogenicity to the liver
3. Greater echogenicity than the liver with maintained corticomedullary differentiation
4. Greater echogenicity than the liver with poor corticomedullary differentiation
5. Greatest echogenicity with loss of corticomedullary differentiation

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**Figure 1: longitudinal scan of both kidneys with good corticomedullary differentiation. (Grade 1)**

Key

Distance AB- Bipolar diameter (renal length)

Distance CD– Antero-posterior diameter (renal width)

Results

Demographic data (Table 1)

A total of 150 adult CKD patients with a male: female ratio of 1.67:1 were recruited. Mean age was 41.59±11.97 years for males and 40.86±12.48 years for females. Hypertension, present in 93 patients (62%), was the leading cause of CKD, including those with hypertension alone or with diabetes mellitus. Mean blood pressure was 151.22±27.92/93.70±18.2 mmHg. Majority i.e. one hundred and thirty-nine patients (92.7%) had elevated serum creatinine (˃1.2mg/dl) while only eleven patients (7.3%) had normal serum creatinine.

Measurements of the kidney’s length were averaged to get the mean (Table 2). The mean renal length and serum creatinine showed a statistically significant negative correlation (r=˗0.275, p=0.001) showing creatinine levels decrease as length increases.

Bivariate correlations were assessed between the dependent variable (serum creatinine level) and each of the independent renal ultrasound parameters (length, echogenicity grade, corticomedullary differentiation) using Spearman's rank correlation coefficient. Spearman’s correlation was chosen as the data were not normally distributed. (It assesses how strongly two variables change together in a monotonic manner, without assumptions of linearity. Values can range from -1 to 1, with -1 indicating a perfect negative correlation and 1 a perfect positive correlation.) Spearman’s correlation between serum creatinine and echogenicity grading showed a positive statistically significant correlation (r=0.572 p=0.0001)

Table 3 shows the results of these bivariate correlation analyses. Higher echogenicity grade correlated positively with creatinine (ρ = 0.572, p<0.001), showing, change is in the same direction. Corticomedullary differentiation also positively correlated with creatinine (ρ = 0.412, p<0.001).

Table 1 Demographic data

|  |  |
| --- | --- |
| Characteristic | n=150 |
| Age (years), mean±SD | 41.6±11.9 |
| Male, n (%) | 94 (62.7 |
| Female, n(%) | 56 (37.3%) |
| BMI (kg/m2), mean±SD | 26.4±5.1 |
| Hypertension, n (%) | 93 (62.0%) |
| Diabetes Mellitus, n (%) | 25 (16.7) |
| chronic glomerulonephritis (CGN) n (%) | 23(15.3%) |
| HIV human immunodeficiency virus associated nephropathy (HIVAN) n (%) | 14 (9.3%) |
| LUPUS-lupus nephritis n (%) | 7 (4.7) |
| Benign Prostatic Hyperplasia; (BPH) n (%) | 1 (0.7%) |
| Non Steroidal Anti Inflammatory Disease (NSAID abuse) n (%) | 2 (1.3) |
| Adult Poly Cystic Kidney Disease (APKD) n (%) | 4 (2.7%) |
| Unknown | 7.94.7) |

**Table 2. Renal length measurements**

|  |  |
| --- | --- |
| **Measurement Mean ± SD / IQR** | **Average kidney length (cm) 10.0 ± 1.7** |
| Right kidney length (cm) :9.8 ± 1.6 |
| Left kidney length (cm) : 10.2 ± 1.9 |

#### Table 3 Comparison of mean serum creatinine levels across the echogenicity grades of the study population

|  |  |
| --- | --- |
| **Echogenicity grades** | **Serum creatinine (mg/dl)**  **Mean ± Standard deviation** |
| Grade 0 | 2.57±2.12 |
| Grade 1 | 4.18±3.53 |
| Grade 2 | 4.47±4.17 |
| Grade 3 | 10.63±6.22 |
| Grade 4 | 11.51±7.30 |

F test=15.765,P -value=0.0001\*

There was also a statistically significant relationship between the categories of corticomedullary differentiation and serum creatinine. (table 4).

The multiple linear regression analysis showed that renal echogenicity was the only predictor of increasing serum creatinine (p<0.05). The coefficient (B) for renal echogenicity shows that, with one grade increase in echogenicity, serum creatinine increases by 2.115 (coefficient =2.115; 95% confidence interval: 0.433 - 3.796) see (table 5).

**Table 4: Comparison of mean serum creatinine level by corticomedullary (CM) differentiation among the study population**

|  |  |
| --- | --- |
| **Corticomedullary (CM)** | **Serum creatinine level**  **Mean ± S.D** |
| Good | 3.68±3.33 |
| Poor | 6.65±5.79 |
| Lost | 10.36±6.97 |

*F-test = 14.636; P-value = 0.0001\**  \*statistically significant

#### Table 5: Multivariate Analysis: Renal Parameters (independent variables) and Serum creatinine (dependent variable)

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Independent variables** | **Coefficient (*B*)** | **95% Confidence interval**  **Lower Upper** | | **P-value** |
| Renal length | -0.660 | -1.633 | 0.314 | 0.176 |
| Renal parenchymal  thickness | -1.272 | -5.550 | 3.006 | 0.548 |
| Renal Echogenicity | 2.115 | 0.433 | 3.796 | 0.016\* |
| Constant | 10.636 | 1.092 | 20.180 | 0.030 |

\*Statistically significant

DICUSSION

The burden of CKD in developing countries is substantial due to the high costs of managing the chronic disease.1,15-17 CKD is a leading cause of morbidity and mortality in our environment, influenced by increasing rates of diabetes and hypertension.1 CKD can be diagnosed through laboratory tests of renal function (serum creatinine, proteinuria, hematuria, urea) or radiological abnormalities.1 This study aimed to identify the renal ultrasound parameter most correlated with increases in serum creatinine in CKD patients.

The mean age of patients in this study was 41.59±11.97 years however the study by Korkmas et al26 showed a mean age of 65.2 years while that done by Singh et al 25 had a mean age of 54.32 years. Patients in the 4th and 5th decade contributed about 57% of the study population in this work. Thus CKD occurs in a relatively younger population as opposed to studies done in other climes where CKD occurred in the older population.11, 26, 25 This may be attributed to the rising incidence of hypertension in younger age groups and with a known black predisposition to hypertension, rising incidence of type 2 diabetes among younger age group and CGN from infective causes in our environment. The study done by Singh et al25 in India showed diabetes as the most known common cause(32%) as opposed to this study where hypertension was the leading cause with an overwhelming 62% followed by diabetes(16.7%). Alebiosu et al26 however found CGN (45%) to be the commonest cause of CKD in our environment followed by hypertension (21%) before diabetes at (13%). Hypertension in CKD can be either a cause or sequelae of the disease and its presence is a poor prognostic factor especially if not well controlled. More males than females were recorded in this study (94 males, 56 females) in a ratio of 1.7:1. This was similar to findings from various studies worldwide 26,27. This may be attributed to differences in physiology between the sexes. Females’ especially premenopausal ones are known to have a slower rate of progression to end-stage disease than men, which could be due to effect of estrogen. Thus, end stage renal disease is commoner in men and men tend to initiate dialysis more commonly than women, 28 and it should also be noted that this study had more patients in the late stages of disease, so this preponderance is not surprising. Stage 3 disease is commoner in females but since at this stage the disease maybe likely asymptomatic and this may explain the fewer number of women in this study.28

Renal length is usually the parameter reported by sonologist and is regarded as a traditional predictor of CKD. 29-30 However, although it is easy to measure, it doesn’t always give a good indication of the size as it doesn’t take into consideration the body habitus of the individual patient. On the other hand, renal volume has been argued to even be a better predictor of size than renal length alone 30, 31 but evaluating the renal volume especially in a clinical scenario is usually difficult because it has to be calculated especially using the ellipsoid formula and the sinus which is not really part of the functional tissue is included in the calculation giving a false increase in volume30.

In this study, most of the patients had normal kidney lengths, with only about a third, having small kidneys and only about 11% had renomegaly. Renomegaly was due to causes such as adult polycystic kidney disease, diabetes mellitus, unilateral kidney and HIVAN which are known causes of increased renal size. Other studies showed the opposite however this could be due to the population in question or the body habitus or the age 24,25This goes to corroborate and supports the views by Milectić et al 34 that relative renal length is better than the absolute renal length. There was a statistically significant negative correlation between the renal lengths on both right and left and mean renal length and serum creatinine. This agreed with others researchers27, however. Singh et al25however, found no correlation between the two variables.

The highest frequency of patients in the study had grade 3 echogenicity followed by grade 4- which represents end stage renal damage. and higher mean values of serum creatinine across the echogenicity grades This was in contrast to the findings by others where patients where the highest frequencies occurred in grade 2 and grade 1 diseases respectively.24, 26 This was attributed to the fact that their studies were based in a referral center and as such most end stage patients had received one form of renal replacement therapy or the other and so were excluded. This study showed an increase in patients with more advanced stages of disease despite it being also done in a referral center and most of the patients were eligible for replacement therapy but were unable to do so due to lack of funds. Also, most patients in our environment usually present very late.

There was a positive statistically significant correlation between the renal echogenicity grades and the serum creatinine levels in CKD patients who partook in this study 25,27. The mean serum creatinine for each grade showed that as serum creatinine increased there was also an increase in renal echogenicity in all the studies. This is important as renal echogenicity is an irreversible finding compared with the serum creatinine which can be reversed with treatment. Using the multiple linear regressions model for the significant variables, it was found that renal echogenicity was the only predictor of serum creatinine. Renal echogenicity is thought to be caused by interstitial fibrosis, sclerosis, focal tubular atrophy, hyaline cast per glomeruli and focal leucocytic infiltration.33 Pävänsalo 34 reported that an echogenic kidney was the most reported finding in CKD and was usually more associated with tubule-interstitial disease; this was also corroborated by Hricac et al33 who observed that the degree of severity of renal echogenicity correlated with the severity of sclerosis and focal tubular atrophy. 34, 35

Cortico-medullary differentiation as a renal parameter seen on ultrasound is closely related to the parenchymal thickness and echogenicity. Cortico-medullary differentiation is best seen in children and the distinction decreases as one gets older.32,35 what is observed in reality is the Sino-parenchymal differentiation, i.e. the parenchyma (medulla and cortex) being distinct

(hypoechoeic) compared to the very echogenic central sinus which contains the calyces and fat.

Cortico-medullary differentiation was lost and poorly maintained in about 4/5th of the study population. This is in keeping with the fact that the bulk of the patients in the study were in grade 3 and 4 echogenicity and advanced CKD. Cortico-medullary differentiation was maintained in only about 1/5th of the study population. Other studies 25-27 showed that the cortico-medullary differentiation was maintained in a greater proportion of the study population (77-90%), this was attributed to the fact that their patients fell into the earlier stages of CKD with earlier grades of echogenicity and thus preserved cortico-medullary differentiation. The differences in the mean serum creatinine across the different categories of corticomedullary differentiation showed a statistically significant relationship. With worsening cortico-medullary differentiation, the mean serum creatinine increases.

In summary, renal ultrasound, particularly echogenicity grading, has prognostic significance through its association with biochemical indicators of chronic kidney disease (CKD) severity. The stratified analysis revealed a significant association between greater echogenicity grades and worsen creatinine levels in advanced stages of chronic kidney disease (CKD). This indicates that renal ultrasound, specifically the evaluation of cortical echogenicity, may aid in identifying individuals who are at the greatest risk of experiencing accelerated disease development and would greatly benefit from intensive treatment or closer observation. Larger prospective cohort studies are needed to validate quantitative ultrasound parameters as surrogate endpoints to guide diagnosis and management globally. Community-based screening with renal ultrasound also merits investigation to enable earlier CKD detection and intervention.

Policy Recommendations:

Governments should increase access to basic ultrasound technology in primary care. Nephrologists and radiologists should collaborate utilizing ultrasonography for CKD monitoring and research. Standardizing quantitative ultrasound reporting could help validate its role in global CKD surveillance.

Limitations:

The referral hospital cohort may not be representative of the general population, as it primarily consists of patients in advanced stages of illness.

Furthermore, the impact of factors such as muscle mass, medications, and comorbidities on creatinine levels has not been fully taken into consideration.

The single-center design and specific demographic characteristics of the tertiary hospital cohort may limit broader generalization until findings are replicated in diverse primary care populations.

While providing potentially useful information, echogenicity grading relies on subjective visual assessment. Inter-observer variability cannot be ruled out despite quality control efforts using standardized scales and blinded reads. Automated image analysis techniques may help address this limitation.

**Line of further research**

Community based case control studies with a larger sample size is advocated.

Multicenter validation of echogenicity grading and other parameters as surrogate endpoints

Studies evaluating ultrasound for guiding therapy in limited resource settings.

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