SONOGRAPHIC RENAL CORTICAL SIGNS PREDICTING RENAL FUNCTION AMONG CHRONIC KIDNEY DISEASE PATIENTS AT MUHIMBILI NATIONAL HOSPITAL

By

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A dissertation submitted in partial fulfilment of the requirements for the award of the degree of Master of Medicine in Radiology of Muhimbili University of Health and Allied Sciences (MUHAS)

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CERTIFICATION

The undersigned certifies that Dr. Kazema R.R has read and hereby recommend for acceptance by Muhimbili University of Health and Allied Sciences (MUHAS) a dissertation entitled: **Sonographic renal cortical signs predicting renal function among chronic kidney disease patients at Muhimbili National Hospital,** in partial fulfilment of the requirements for the degree of Master of Medicine - Radiology of Muhimbili University of Health and Allied Sciences.



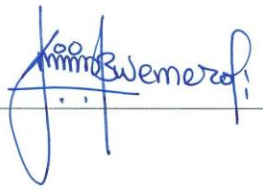
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trying moments. Our Daughter, Joan always cheered me up at moments when I felt low and exhausted. I also thank the Almighty God for blessing us with a second daughter, Grace, during these years of my post graduation.

DEDICATION

This dissertation is dedicated to my dear Brother and his lovely family, his wife Grace Nanyangwe, sons George and Mibazi, and their daughter Tibela. It is also dedicated to the memory of my late father namesake, Mr. Joel Nshekanabo Bwemelo who inspired me right from childhood to work hard.

ABSTRACT

Objective: To determine whether renal sonography pathological changes can be used to predict renal function among patients with chronic kidney disease (CKD).

Methods: This was a cross-sectional study which evaluated 145 patients with CKD who underwent both kidney sonography and renal function test based on estimated glomerular filtration rate (eGFR) by MDRD equation. These patients were recruited from Diabetic, Hypertensive and Nephrology clinics at Muhimbili National Hospital from June to December 2009. A systematic random sampling was used based on the fore mentioned clusters (*Diabetic, Hypertensive and Nephrology clinics*). Hricak standardized measure of renal cortical echogenicity scoring was used as Grade 0; Grade I; Grade II and Grade III. Cortical volume was also calculated and obtained as a renal volume minus central echogenic complex (sinus) volume. These three variables were analyzed looking for correlation, sensitivity, specificity, positive and negative predictive values and Likelihood Ratio. Renal function test using eGFR by MDRD equation was used as the gold standard.

Results: The regression correlation between renal cortical echogenicity and renal function (eGFR) revealed a correlation coefficient of $r^2 = 0.622$, $p<0.001$. The sensitivity of echogenicity as predictor of renal function was 74.7% (95% CI: 0.68 - 0.78), specificity was 93.5% (95% CI: 0.85 - 0.99). Positive Likelihood Ratio (LR) +11.6; $p<0.001$), hence echogenicity proved to be a strong prediction sign. To be more precise, it was shown that cortical echogenicity grade I or below shows renal function of more than 60 mL/min/1.73 m^2 and echogenicity grade II or more presents with a compromised renal function below 59 mL/min/1.73 m^2

Right and left renal cortical volume as relates to estimated GFR showed correlation coefficient of $r \approx +0.49$ and $r \approx +0.43$ respectively. It revealed within +0.7 and +0.3 range which defines a weak linear association. It showed the regression slope **b** with (95%CI: 0.50-1.04) and correlation coefficient of $r^2=0.184$; $p<0.001$.

Conclusions: The observed correlations between renal cortical echogenicity, renal cortical parenchyma volume change and renal function estimated by GFR suggest that:

1. Renal cortical echogenicity sign may potentially be useful as surrogate marker of the renal function.

2. Renal cortical volume as a predictor of renal function did not qualify our alternative hypothesis.

3. At present however, precise prediction of renal function based on a renal cortical volume change requires a big sample size for the specific conclusion since its significance testing shows a confidence interval with high prediction variability.

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LIST OF ABBREVIATIONS

1. BUN :Blood Urea Nitrogen
2. CBC :Complete Blood Count
3. CKD :Chronic Kidney Disease
4. CLcr :Creatinine clearance
5. CMD :Cortico-Medullary Differentiation
6. CRF :Chronic Renal Failure
7. CSR :Cortico-Sinus Ratio
8. DPD :Diffuse Parenchymal Disease
9. DRPD :Diffuse Renal Parenchymal Disease
10. eGFR :estimated Glomerular Filtration Rate
11. GFR :Glomerular Filtration Rate
12. Hb :Haemoglobin
13. HIV :Human Immune Deficiency Virus
14. MDRD :Modified Diet for Renal Disease
15. MHz :Megahetz
16. MNH :Muhimbili National Hospital
17. MUHAS :Muhimbili University of Health and Allied Sciences
18. RCE :Renal Cortical Echogenicity
19. RFT :Renal Function Test
20. RPW :Renal Parenchymal Width
21. SPSS :Statistical Package for Social Science
22. USG :Ultrasonography

DEFINITION OF TERMS

Biometry: Application of statistics, mathematics, systems analysis, operations research, computer science, and other areas to studies of the life sciences.

Echogenicity: The characteristic ability of a tissue or a substance to reflect sound waves and produce bright echoes. Less reflecting tissue and high reflecting tissue both exhibit hypoechogenic and hyperechogenic pattern respectively.

Kidney Failure: The kidney of GFR less than 15 ml/min/1.73 m^2 which in most cases is associated with signs and symptoms of uraemia. It requires dialysis as a temporary measure and kidney transplant as a definitive treatment.

Glomerular Filtration Rate (GFR): The amount of blood plasma filtered as it flows through the glomeruli. It is the scan of all single nephron on both kidneys with a typical normal range of 90-120 ml/min.

MDRD: Modification of Diet in Renal Disease, it is the study equation used to estimate glomerular filtration rate (eGFR) as a marker and an approach used to define disease threshold and its stages for chronic kidney diseases.

Chronic Renal Failure (CRF): This is the syndromic stage of chronic renal disease (CKD) associated with anaemia, uraemia, hypocalcaemia and hyperphosphatamia. It is the stage requiring dialysis and renal transplant.

Chronic Kidney Disease (CKD): This is the progressive kidney damage with a GFR of 60 ml/min/1.73 m^2 or less that has been persistent for more than three months.

INTRODUCTION

Chronic kidney disease (CKD) is a slow progressive loss of kidney function over the span of years (1;2) as the internal structures of the kidney are slowly damaged. CKD can range from mild dysfunction to severe kidney failure consequently resulting into permanent kidney shut down (2) called Chronic Kidney Failure (CKF)(3). Chronic kidney disease is common and may go undiagnosed until the process is far advanced and its failure is on the horizon, CKD presents with permanent reduction in glomerular filtration rate (GFR) (1;4) sufficient to produce detectable alterations in well-being. Usually occurring at an organ function of eGFR below 59 ml/min/1.73 m^2 (5).

CKD often results from any disease that causes gradual loss of kidney function. The most common causes of chronic renal disease are diseases that damage the kidneys little by little for many years which include high blood pressure and diabetes mellitus (6). Others are Glomerulonephritis, Sickle cell nephropathy, Interstitial nephritis (7), Polycystic kidney disease, obstructive uropathy, analgesic abuse (8), Systemic Lupus Erythematosus (SLE), HIV nephropathy and diseases of the heart or lungs.

There are five stages of decreased renal function categorized by estimated GFR among patients with CKD (1;4). The five recognized stages are:

1. proteinuria with normal eGFR of more than 90ml/min/1.73 m^2
2. eGFR from 89 to 60 ml/min/1.73 m^2
3. eGFR from 30 to 59 ml/min/1.73 m^2
4. eGFR from 15 to 29 ml/min/1.73 m^2
5. eGFR less than 15 ml/min/1.73 m^2

These five categories of CKD from Kidney Disease Outcomes Quality Initiative guideline have been widely accepted and used as universal screening tools (9). Currently, many laboratories report the estimated GFR (eGFR) for all patients' samples requesting serum creatinine (10). These stages are ideally based on the gradual accumulation of urea (Uremia). Uremia is a term applied to the clinical manifestations of renal dysfunction seen in stages 3, 4 and 5 as outlined, while stage 1 and 2 are regarded as stable renal function.

Ultrasound is the basic investigation for most of patients attending medical clinics and its role is doubly important for patients with diffuse renal parenchymal disease especially CKD (11),(12). Ultrasonography is employed increasingly as a screening test and it is very useful when used as a follow-up technique to detect complications and assess renal disease remission. However, it is important to note that ultrasound may be totally normal (11;13) in cases of acute diffuse renal parenchyma disease, hence complementary examinations like renal biopsy (13), renal function test (eGFR) and renal scintigraphy are still necessary.

Ultrasound is reliable (14), fast and easy modality in detecting renal parenchymal pathology. It can assess echotexture, the size, outline and shape of the kidneys and some causes of diffuse renal parenchymal disease. Evaluating renal conditions and carrying out measurements to obtain renal cortical echogenicity and volume ultrasonography (USG) stands as an ideal examination, as it provides accurate measurements. Kidney can be easily visualized and USG may provide limited spectrum of anatomic variation and pathological changes. In addition, the examination is quite simple, safe and cost-saving (12). Today, ultrasound is one of the most commonly used diagnostic tool (12) the reasons being, it is non-invasive and widely available.

The qualitative assessment of the echogenicity of the renal cortex and the medulla is one of the most important diagnostic criteria in the assessment of diffuse renal parenchyma disease (11;15-18). Changes in the echogenicity of the renal cortex suggest changes in renal biometric cortical structure as well as renal function (17-19). Renal function in the form of Glomerular filtration rate (GFR) is an important test for kidney function and its knowledge in relation to renal cortical echogenicity can be essential to the diagnosis and management of chronic kidney disease (CKD).

CKD causes renal biometric changes over time along its course. These structural changes alter the main function of the kidney which is to produce urine and maintain homeostasis through the excretion of metabolic waste products. The volume of each kidney reflects renal mass, which contains more than one million microscopic renal functional units (nephrons) existing in renal parenchyma (12;20).

Renal parenchyma comprises renal cortex and medulla, in which filtration process takes place in renal cortex and reabsorption occurs in the medulla. These two important functional areas are mostly affected by CKD etiological diseases. Renal function is affected by the existing surface area or volume in renal parenchyma where the filtration process takes place. It is important to note that renal parenchymal volume relates to renal functional capacity, since renal parenchyma diseases affect both renal function and renal cortical volume simultaneously. In ultrasonography, when focusing on renal diseases the pathological renal changes due to above outlined etiologies reveal a similar pattern and are termed as Renal Parenchymal Diseases (RPD) (11). Sonographically all etiologies causing CKD are collectively termed as Diffuse Renal Parenchymal Diseases (DRPD).

Estimated GFR (eGFR) is the pillar of CKD diagnosis, staging and management. Serum creatinine measurement, a widespread test of kidney function is insufficiently sensitive to detect moderate CKD and is affected by a range of non-renal influences. An alternative solution is to measure serum creatinine and estimate GFR using MDRD equation which corrects with some of the more significant non-renal influences like sex, ethnicity, age, and serum protein.

This alternative way of using GFR in CKD is known to be more sensitive for the detection of CKD than serum creatinine and more accurate than creatinine clearance. This research therefore, tested the applicability of Ultrasonography as an alternative investigation to predict renal function among CKD patients. Cortical echogenicity appeared to be a good sonographic sign that can be used to predict renal function and renal cortical volume needs more evaluation. Both sonographic signs were validated against renal function gold standard eGFR.

LITERATURE REVIEW

Renal Parenchyma Echogenicity:

Sonography has an increasingly important role in the evaluation of urinary tract disease in all ages. Knowledge of normal renal parameters is essential for the accurate evaluation of abnormal kidneys, since renal parenchymal echogenicity and renal sinus echoes vary with age (21). The appearance of normal kidneys on sonograms in newborn and young children is unlike that of older children and adults. However by 7 months, the child renal parenchyma shows the adult pattern and renal parenchyma echogenicity of the renal cortex is usually less than that of the liver in healthy subjects (22).

It is now known that quantification of renal cortical echogenicity is feasible, reproducible and may be useful in detecting and following up renal diseases (22). Renal cortical echogenicity is normally lower than the echogenicity of liver, spleen and renal sinus (13). Renal sinus appears more hyperechoic when compared with renal parenchyma because of the presence of hilar adipose tissue with fibrous septae, blood vessels and lymphatics (23). Chronic renal parenchymal diseases and increased renal cortical echogenicity directly correlates with diffuse renal parenchyma diseases. In addition, a highly echogenic cortex has been shown to be the most common abnormality in patients with diffuse parenchymal renal diseases (24). Renal parenchyma echogenicity, quantitatively and qualitatively is graded in comparison with the liver (17;25-27).

Presence of concurrent fatty liver infiltration, is associated with false positive cortical echogenicity (25;26), hence fat liver patients are excluded. When liver parenchyma appears hyperechoic on ultrasonography, spleen echogenicity is used as a standard reference. However, kidneys may be isoechoic to the liver even when there is no clinical or laboratory evidence of renal disease (17;25). Despite sonography providing high positive predictive value for renal parenchymal disease, specific diagnoses cannot be distinguished by sonographic characteristics. However, quantification of renal cortical echogenicity increases the utility of this measure in the diagnosis of diffuse renal parenchymal diseases. Renal echogenicity is graded according to a standardized score with four categories (26;27):

1. Grade 0: indicates the renal cortex being less echogenic than the liver
2. Grade I: indicates the renal cortex and liver being equally echogenic
3. Grade II: indicates the renal cortex being more echogenic than the liver and
4. Grade III: indicates the renal cortex and renal sinus being equally echogenic.

The use of standardized method in measuring renal echogenicity has the potential to enhance diagnosis of patients with kidney diseases, particularly in patients whom renal biopsy is relatively or absolutely contraindicated. It may, in cases of the most severe echogenicity, permit a presumptive diagnosis of renal parenchymal diseases. Conversely, in cases of those with the lowest level of echogenicity, it may exclude the diagnosis without a biopsy (23;24;27).

It has been shown to be a positive correlation between kidney-liver echogenicity ratio and serum creatinine concentration in glomerulonephritis with or without renal failure ($p < 0.001$) (28). These results suggest that the degree of increased renal echogenicity reflects the severity of the renal disease and the kidney-liver echogenicity ratio measured quantitatively may provide an additional simple noninvasive method to monitor the progression of glomerulonephritis. Another study on postnatal renal sonography showed that increased renal parenchymal echogenicity on postnatal ultrasonography is a strong predictor of a compromised renal function. Increased echogenicity on ultrasonography yields a sensitivity of 100% and specificity of 99% for predicting relative renal function. It is therefore, concluded that increased renal parenchymal echogenicity can be used as a predictor of impaired relative renal function (29).

Among literatures reviewed, the comparison of renal parenchyma echogenicity as a predictor of renal function has been extensively studied through all ages (23;24;27-29). Most studies here concentrated mainly on comparison between renal function test assessed by serum creatinine and renal parenchymal echogenicity grades, little is known on renal function test assessed by eGFR in relation to renal parenchyma echogenicity. It is documented that eGFR is the best test for renal function and has potential to monitor

disease progression, prognosis, dosing and follow up. Therefore, sonographic characterization of renal parenchyma echogenicity versus eGFR raises many questions to researchers, as it has been done on serum creatinine. Renal parenchyma echogenicity as it does eGFR is stated to be a sensitive sonographic sign for diffuse renal parenchymal diseases (23;24;27-29). This research, evaluated these two important variables to not only bridge the gap but also to examine if cortical echogenicity can faithfully predict renal function.

Renal biometry

Determination of renal parenchymal volume in healthy individuals is rarely carried out as it needs several calculations; it is therefore regarded as unpractical in daily clinical setting. However, in certain conditions it can be used to estimate nephron capacity as a representation of renal functional capacity. In abnormal condition such as renal failure, the measurement of renal parenchymal volume provides a more accurate parameter in estimating renal size and function than renal length only (30). Renal parenchymal volume depends largely on the difference between renal volume and renal sinus volume in the central echogenic area (31).

The volumes of kidney, central echogenic area, and right and left renal parenchymal volume are measured using the following formulae (31):

1. Renal volume = length (L) x width (W) x thickness (T) x 0.523,
2. Central echogenic volume = (L x W x T) of central echogenic area x 0.523,
3. Renal parenchymal volume = renal volume - central echogenic volume.

The length of both kidneys in adults is considered normal when it is between 10cm and 13 cm being the longest distance from the upper edge of renal upper pole to the lower edge of renal lower pole at longitudinal section. The difference of right and left renal length should not exceed 2 cm, the left kidney being longer (13;31).

It is generally agreed that normal renal parameters correspond to somatic parameters, normal values thus determined serve as a baseline to study renal growth and detect an abnormality with a greater degree of confidence(32). Despite the limited studies on renal parenchymal volume, the few available studies have shown the normal average value of renal parenchymal volume in health adults to be 88.04 cm^3 for the right kidney and 115.13 cm^3 for the left kidney (33). Another study showed an average value of healthy renal parenchymal volume of the right and left kidney to be 80.1 cm^3 and 85.2 cm^3 respectively (34). These two studies show a big variability of the left kidney cortical volume that has been explained by two reasons: first, as the spleen is smaller than liver, the left kidney has more space to develop and second, the left renal artery is shorter and straighter than the right renal artery, leading to larger amount of blood flowing to left kidney leading to more nutrition.

Despite ultrasound having unlimited role in diagnosing intrinsic parenchymal renal disease but can assess size and shape precisely. It has been also shown to have a sensitivity of 62–77%, specificity of 58–73% and a positive predictive value of 92% for detecting microscopically proved renal parenchymal changes (18). In chronic kidney disease, there is increased fibrosis of the renal cortex, these fibrous tissues reflect sound waves, and causes increased echogenicity on renal ultrasound. Fibrosis causes kidney to shrink leading to less than 10 cm long, this suspects chronic scarring resulting in shrinking of the kidney (35).

Renal biometric changes are on widespread use as the diagnostic yield of ultrasonography to detect early signs of reduced renal function. Renal parenchymal volume change in particular when shown by ultrasonography it can detect early reduced renal function, since reduced renal parenchymal volume may occur prior to elevation of serum creatinine. This biometrical renal change, if carefully noted on routine ultrasonographic examinations are suspicious indicator of renal compromise especially in elderly (36).

Ageing is associated with a progressive loss of renal mass and kidney length and a decline in glomerular filtration rate (GFR) as it does in chronic renal parenchymal disease due to parenchymal fibrosis. Renal function and kidney size measured by ultrasonography significantly correlates with GFR ($r=0.46$; $p=0.02$), denoting the potential prediction of renal function by volume change (35). A significant relationship between renal parenchymal volume and kidney function measured by eGFR was also observed among 26 children with recurrent urinary tract infection (37). This study concluded that renal parenchymal volume is a reliable method for evaluating glomerular filtration rate.

Renal Function Test: ***the use of eGFR:*** GFR is usually accepted as the best overall index of kidney function in health and diseased patients. Normal GFR varies according to age, sex, and body size, in young adults it is approximately 120-130 mL/min/1.73 m^2 and declines with age. A decrease in GFR precedes the onset of kidney failure; therefore a persistently reduced GFR below 60 mL/min/1.73 m^2 is a specific diagnostic criterion for CKD (10).

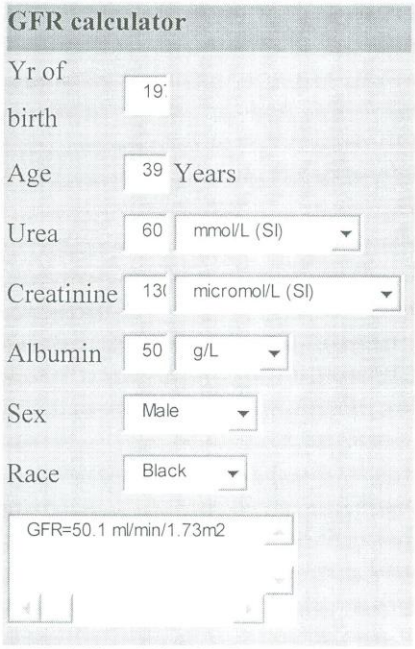
The most common measure used to assess overall kidney function is the serum creatinine concentration expressed as renal serum creatinine clearance (CLcr) (38;39). However, interpretation of this index is complicated as it is inversely proportional to the GFR and varies between individuals based on differences in age, diet, sex and muscle mass (38;39). The use of serum creatinine concentration alone to assess kidney function results into false negative of 25% undiagnosed cases of CKD (40). For this reason, the broader use of serum creatinine concentration as a tool to increase the detection of asymptomatic CKD is therefore nonspecific.

GFR can be calculated from the results of blood creatinine, age, race, gender and other factors like BUN and serum albumin as it tells the stage of kidney disease and helps to plan management. Estimation of GFR (eGFR) can be calculated by the following equation, Modified Diet for Renal Disease (MDRD) formula. MDRD is widely recommended for routine use and may be reported with all requests for serum creatinine aiming at staging and patients follow ups (38;39). Another widely used equation to estimate GFR is the "Cockcroft and Gault equation" which requires patient age, sex,

weight or height, and serum creatinine, which is mainly recommended for drug dosing decisions (38).

MDRD equation has gained superiority over Cockcroft–Gault equation, the later requires additional information such as body surface area based on height and or weight measurements which lead to additional complexities and limits its wider use. Direct comparison of the MDRD equation with Cockcroft–Gault equation from 24-hour urine collections have shown the MDRD equation to be superior for estimating GFR, particularly in the range GFR < 60 mL/min/1.73m^2 (39).

MDRD formula has not been validated in children and its use is restricted to people over 18 years of age (40;41). MDRD equation has been validated in many clinical situations (5), it estimates GFR adjusted for body surface area but spells differently in each sex and race. The 6-variable MDRD study equation calculator for eGFR used in this research is:



6-Variables MDRD formulae:

170 (Cr $^{-0.999}$ **x** age $^{-0.176}$) x BUN$^{-0.170}$ **x** alb$^{-0.138}$ **x** (1.178 *if black*) **x** (0.822 *if female*)

Source: *www.renal.org/Resources/MDRD-GFRcalculator.*

The possibility of determining the correlation between ultrasonographic kidney sizes and glomerular filtration rate (GFR) by ultrasonography employs an easy and less demanding type of investigation for renal function establishment. Kidney sizes, especially the kidney length, correlate with GFR (42). With this observation, it was worth noting that kidney sizes assessment by ultrasonography may play a role in renal function evaluation.

Glomerular filtration rate (GFR) is affected by the existing surface area in renal parenchyma where the filtration process takes place (20). The measurement of multi dimensional renal parenchymal area provides a more accurate estimation of renal function compared to one-dimensional renal measurement only for example length (12;43).

PROBLEM STATEMENT

Chronic kidney disease (CKD) is a serious cause of morbidity and mortality worldwide, prevalence of CKD in United State adult is estimated to be 11% (40). In Australia, the general population study shown 11.3% of adults having eGFR below 60 mL/min/1.73m^2. More than 10% of the Kinshasa, Congo (DRC) population exhibits signs of CKD which is affecting adults in their productive years. Risk factors identified for CKD in these studies were hypertension, diabetes and obesity (40;44;45).

Currently, in Tanzania little is known on the magnitude of CKD in terms of common etiological factors, modes of management and treatment outcomes, but it is well known that metabolic diseases like Diabetes, Hypertension and their complications are on alarming increases which are the potential causes of CKD (46).

It is therefore, concluded that CKD is common and warrants improved early detection and classification to improve management and its outcomes. Focus being on reducing mortality in people with CKD, who actually have 20-fold greater chance of death mainly from cardiovascular complications before they get an opportunity for kidney transplant (47). High prevalence of HIV- associated nephropathy worsens the situation in HIV endemic area like Tanzania. Prevalence of CKD among HIV patients in western Kenya was estimated by the Cockcroft-Gault equation to be 11.5% (48).

CKD is frequently asymptomatic and many afflicted people have significant reduction of kidney function without overt urinary abnormalities (44). Therefore, progression to end-stage may be halted or slowed down when kidney damage is detected at an early stage and treated. In view of this, there is a need for a quick, reliable, cheap, non invasive and simple investigation that would help in the screening and staging process for the kidney ailment, which can be achieved through a frequently done investigation, like an ultrasonography.

RATIONALE

In developing countries where resources are still limited, a widely available modality like ultrasound can be wisely used to establish a suspicious message on renal deterioration. Ultrasound can be used also in early workup, monitoring aiming at reducing disease progression, morbidity, mortality, and save cost related to dialysis and kidney transplant.

Many studies have been done on correlating sonographic renal changes with renal function by using serum creatinine as a functional mark of renal failure (1;12;13;23;49), but none of these correlated eGFR with sonographic findings. Since serum creatinine portrays non specific measure on detecting renal dysfunction, therefore Glomerular filtration rate (GFR) a Gold standard test of kidney function is to be used in this research.

In a busy clinic with poor infrastructure, measurement of GFR may look technically demanding, expensive, time consuming and unsuitable for routine screening. Established sonographic criterion to mark renal function based on gold standard eGFR stages provides important information which clinicians can depend upon to predict renal function of an individual. This may ultimately reduce cost and time to both patients and clinicians from the highly demanding eGFR.

It is of our great advantage today that ultrasound facility is widely available, easily done, cheap and noninvasive diagnostic guidance available. Ultrasonography can also be an important screening tool for CKD stage 3, 4 and 5 so that complications can be anticipated and prevent progression to CKD, thus reduce the need of dialysis and kidney transplant.

These study findings are the challenge to Nephrologists, Radiologists and medical community at large who may find it necessary to study more on renal function as it is predicted by renal pathological sonographic signs.

OBJECTIVES

Broad Objective

To determine the precision of sonographic renal parenchyma changes in the prediction of renal function among patients with chronic kidney disease attending Nephrology clinic at Muhimbili National Hospital, July to December, 2009.

Specific Objectives

The specific objectives of the study are:

1. To determine relationship on renal parenchyma echogenicity grades and eGFR.
2. To determine the relationship between renal parenchyma volume and eGFR
3. To validate both renal echogenicity and volume change in relation to eGFR

HYPOTHESES

In this study, it is hypothesized that:

1. *Null*: (H_0)

   There is no significant difference in estimating renal function among CKD patients by using ultrasonographic renal cortical signs or eGFR.

2. *Alternative*: (H_1):

   Renal ultrasonographic signs can be used to predict renal function among CKD patients.

METHODOLOGY

Study Design:

This was an observational cross-sectional descriptive study.

Study Period and Study Area:

This study was conducted in six months duration, between July and December, 2009 at Muhimbili National Hospital Nephrology clinic in new outpatient department (OPD) complex. The clinic is specialized for patients with diagnosis of chronic kidney disease. Patients who attend this clinic come from different parts of the country. The clinic normally operates one day per week for eight hours with an average of 20 – 30 follow up cases and new cases.

Study Population:

All patients attending Nephrology clinic at Muhimbili National Hospital with chronic kidney disease were eligible for the study after all exclusion criteria have been ruled out.

Inclusion Criteria:

All patients with chronic kidney disease secondary to diffuse parenchymal insults like:

- Diabetes
- Hypertension
- HIV/AIDSG
- Glomerulonephritis
- Drug toxicity
- SCA etc were included
- The age limit ranged from 20-60yrs (48), this age limits the extremes into which the kidneys grow to its maximum size (9-13cm) and gradually start to decrease in size from the age of 60years.

Exclusion criteria:

The following were excluded in the study:

- Patients who did not consent
- Sick patients with difficulties to move through labs during study investigations
- Obese patients with fatty liver as it interferes with right renal reflectivity
- Obstructive uropathy like hydronephrosis
- Cancer of urinary system
- Renal stones
- Congenital abnormality like polycystic kidney disease

Sample Size Estimation: Considering the study power of 95%, a random likely error is estimated to be 0.05. The sample size of 138 patients were estimated based on the Kinshasa (45) community prevalence of chronic renal disease. The standard sample size estimation (Kish & Leslie) formula is: $\mathbf{N = z^2p\ (1\text{-}p) \div E^2}$ Where by: **Z**- is the point of normal distribution corresponding to the significance level 1.96; **p**-prevalence from the pilot study in Kinshasa 0.1; **E** -maximum likely error 0.05. From this formula the sample size was calculated as follows: $\mathbf{N = (1.96)^2 X\ 0.1(1 - 0.1) \div (0.05)^2 \approx 138}$

Sampling Technique:

Nephrology clinic has about 260 patients with CKD, who attend the clinic once a month or more as per clinical review demands. During this study a patient's appointment list was obtained and the number of patients listed from each visiting dates. A systematic random sampling was used from which six patients were selected per day; every fifth patient was recruited from the clinic list of thirty patients. This was done for consecutive six months to obtain a sample size of 144. This randomization was carefully done to include new cases and not to repeat patients who have been previously studied, it was checked by asking the patient if he or she has been involved in this study. Other mechanism used to avoid repetition was a red mark at the top of each studied case note (patient file)

Data Collection:

Following the nature of the study, data were collected through structured closed ended questionnaire gathering demographic factors, laboratory variables and Ultrasound variables. Demographic factors were gathered from the patient case note, which included age, sex, race, primary diagnosis, treatment information and co morbid diseases.

Blood samples were collected on the same day of the patient sonography and their analysis was done by the same laboratory machine throughout the study. The comprehensive chemistry panel (CCP) was done and urea, creatinine, albumin levels obtained were substituted in the MDRD formulae to establish the renal function by eGFR then transferred to the questionnaire.

Sonographic images were produced by Philips HDI4000 machine from Best Eindhoven, Netherland. The study used broadband curve-linear transducers of 2MHz to 5MHz range which is in a routine use at the Department of Radiology. Sonographic images of renal-hepatic-spleen echogenicities grades of right and left kidney cortex were performed using a B mode scans. Visual grades interpretation was done on a freezed image by comparing right kidney to the normal liver and left kidney to the normal spleen on the same scan. Images obtained were printed on a thermal paper, qualitatively compared by two observers to minimize observer bias. Renal cortical volumes from three measurements of individual kidney and sinus were obtained: length, width and thickness from which volumes were calculated. Echogenicity grades and cortical volumes were transferred to the questionnaire.

Data Analysis:

All filled closed ended questionnaires were given an identification number, coded and screened before entering into the statically package for social science (SPSS). Qualitative data were analyzed and interpreted through a description while quantitative data were tabulated, analyzed, correlated and interpreted according to the result obtained.

Relationship between the two tests *(Cortical echogenicity/cortical volume and eGFR)* was determined. Pearson and linear regression were used; sensitivity, specificity and likelihood ratio were computed accordingly. P-value of < 0.05 was considered significant.

Ethical Considerations: Ethical clearance was obtained from MUHAS - IRB (Institutional Review Board) and permission to conduct the study using the Nephrology clinic, imaging facility and the laboratory was obtained from the Director of clinical services of MNH. An informed consent (verbal and written) was provided to patients. Confidentiality was observed during patient interview, collecting specimen, and performing abdominal ultrasonography. Whenever it deems necessary, physical examination was done. Patients who were entitled but refused to participate in the study were attended as usual. The objectives and procedure to be followed in this study were clearly explained to all participants.

RESULT

Demographics and Clinical Characteristics:

A total of 145 eligible patients consented to participate in this study, from these 83 (57.2%) were males and 62 (42.8%) females. The study sample age group ranged from 20years to 60years with a mean age of 40years.

Among the studied population, 72% had long standing hypertension and or diabetes. Cause(s) of CKD among 17% of the study sample were not yet established at the time of this research, while 11% were diagnosed HIV nephropathy with established chronic kidney disease. Variables assessed from this research were (*Renal cortical echogenicity grades and renal cortical volume*).

The third dependent variable was the estimated GFR (*eGFR*), from eGFR, this research results intended shows the relationship(s) with the stated independent variables. The ultimate goal was to establish an alternative use of sonographic signs to predict renal function among patients with CKD.

Sonographic Characteristics

Renal cortical echogenicity

Renal cortical tissue characterization was performed and the distribution of echogenicity scores was as follows. Grade 0 (27.6%); Grade I (26.9%); Grade II (33.8%); and Grade III (11.7%) as shown by *table: 1 below*.

Table: 1. Right and Left kidney cortical echogenicity score distribution (n=145)

Echogenicity	Right kidney		Left Kidney	
	Frequency	Percentage in %	Frequency	Percentage in %
Grade 0	40	27.6	41	28.3
Grade I	39	26.9	38	26.2
Grade II	49	33.8	49	33.8
Grade III	17	11.7	17	11.7
Total	145	100.0	145	100.0

Pearson's correlation coefficient of r = 0.997; p<0.001 shows that echogenicity change among CKD patients occur simultaneously bilaterally and symetrical.

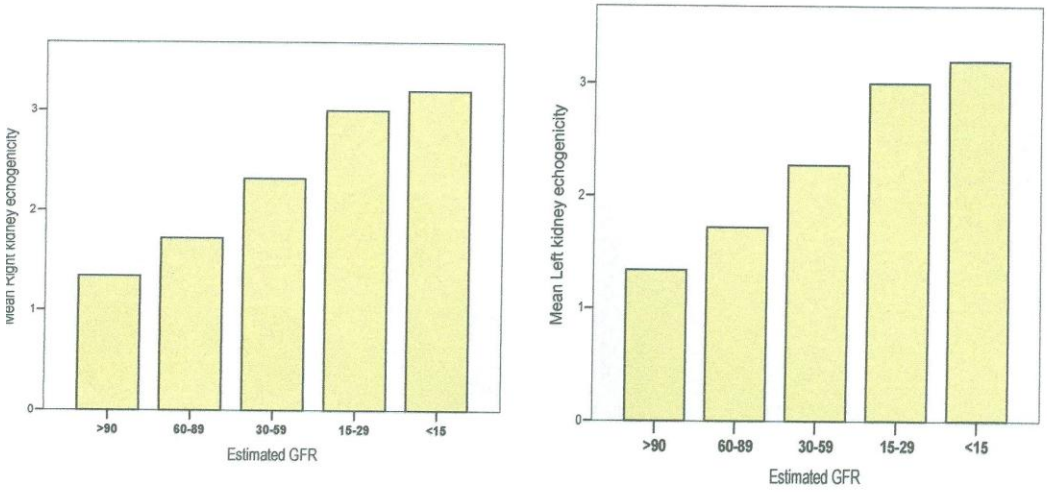
Table: 2: Right kidney echogenicity with estimated GFR (n=145)

Echogenicity	Estimated GFR					Total
	>90	**60-89**	**30-59**	**15-29**	**<15**	
Grade 0	30	8	2	0	0	40
Grade I	13	7	11	2	6	39
Grade II	1	3	9	11	25	49
Grade III	0	0	0	2	15	17
Total	44	18	22	15	46	145

This table reflects an interval deterioration of renal function with concurrent increase in renal cortical echogenicity, it is hypothetically shown through the cells left to right diagonally.

The right kidney is taken as a representative since there is no echogenicity difference noted among the two kidneys during scanning (*table 1*).

Figure: 1. Right and Left cortical reflectivity as a function of estimated GFR (n=145)

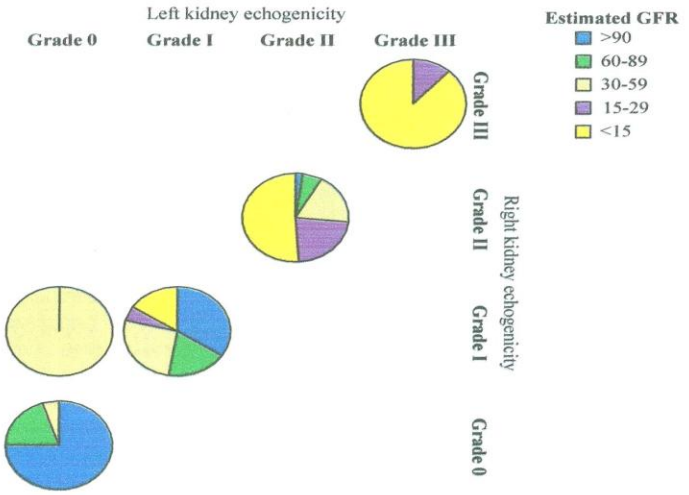


The linearity of renal cortical echogenicity shows deterioration of renal function estimated by eGFR from right and left cortical echogenicity histograms.

Pearson's correlation coefficients of right and left renal cortical reflectivity are ($r \approx +0.79$) and ($r \approx +0.78$) respectively, $p < 0.001$.

Histograms similarity from right and left kidney echogenicity scores in relation to eGFR shows the likelihood that, right and left cortical reflectivity supports our alternative hypothesis.

Figure: 2: Combined right and left kidney echogenicity with estimated GFR (n=145)

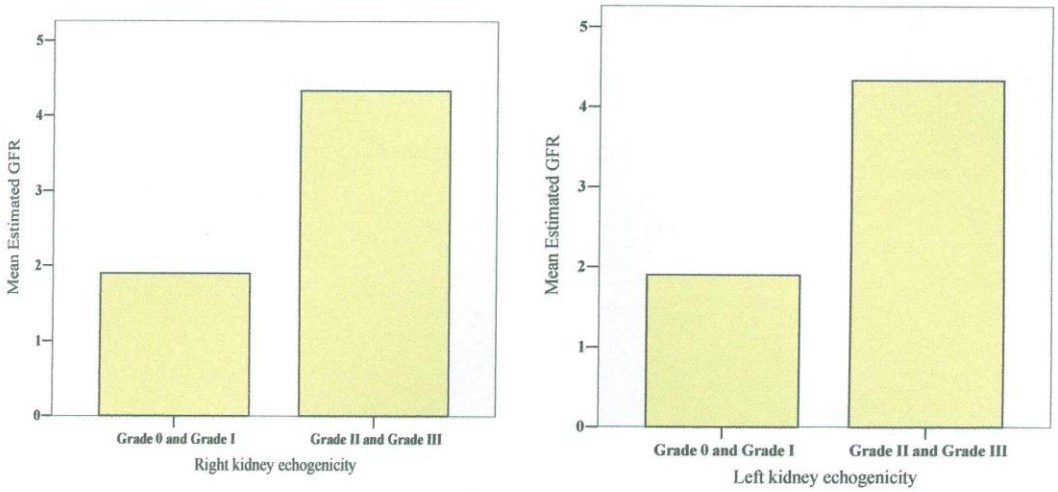


This schematic correlation between combined right and left cortical reflectivity verifies a linear deterioration of eGFR. It is shown by systematic thinning and opening out within pie colors presenting renal function as kidney cortical echogenicity worsen towards grade III cortical reflectivity.

Red colour presents a stable renal function of >90 ml/min/1.73 m^2 which hardly extends beyond echogenicity grade I and yellow colour presents poor renal function which widens bigger at grade III cortical reflectivity.

It demonstrates that, if patients with CKD are selected at random more than 90% of patients having cortical echogenicity grade II will be having eGFR of less than 59 ml/min/1.73 m^2

Figure: 3. Combined cumulative effect of cortical echogenicity on eGFR (n=145)

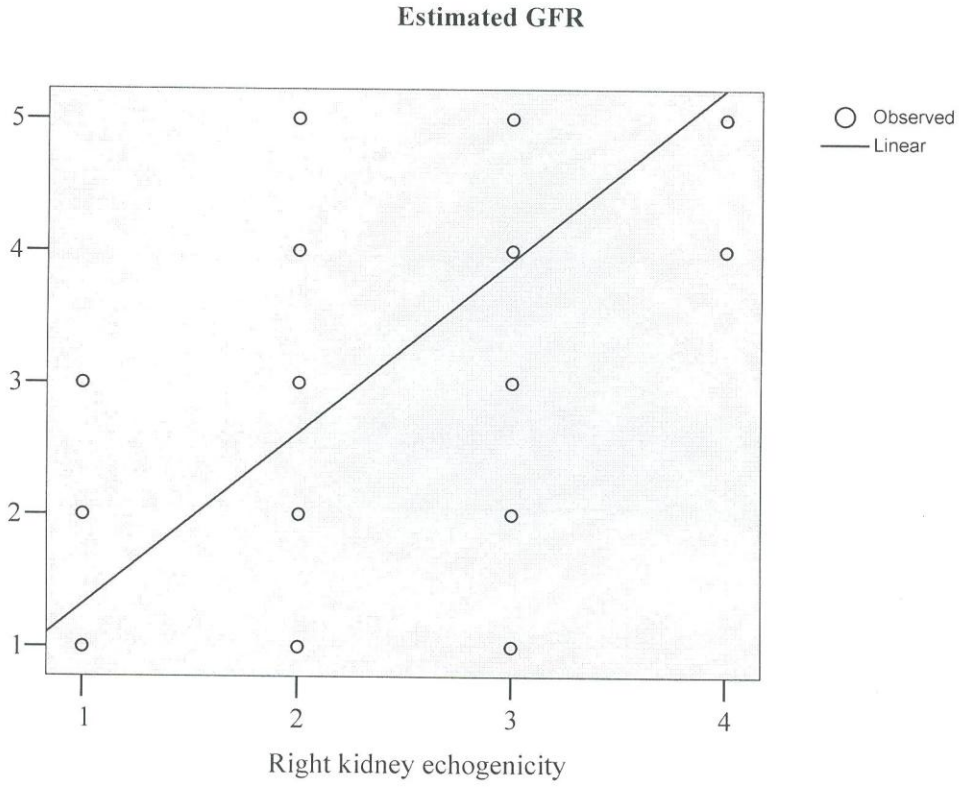


Amplification of the researched characteristic can be very impressing when the effect is obviously appreciated. When combined right and left renal cortical reflectivity, grade 0 combined with grade I and grade II combined with grade III show additive effect of cortical echogenicity phenomenon challenging renal function estimated by GFR.

It is shown clearly that cortical reflectivity may hardly go beyond grade I if the renal function is within stable parameters of more than 60 ml/min/1.73 m^2.

However, the tremendous surge of grade II when combined with grade III cortical echogenicity reveals a good widow between stable and poor renal function. It is this window from which ultrasound can easily use to differentiate between stable patients and those who need urgent referral to Nephrologist.

Figure: 4: The eGFR and renal cortical echogenicity regression correlation (n=145)



Simple linear regression correlation between renal cortical echogenicity and renal function (eGFR) shows correlation coefficient $r^2 = 0.622$, $p<0.001$.

Despite of these data being grouped (categorical) the scatter diagram shows a well best fit line that cuts the data equally showing its linear relationship between the variables.

Table: 3. Likelihood that cortical echogenicity predicts renal function (n=145)

Combined eGFR in	Right renal cortical echogenicity		Total
mL/min/1.73 m^2	Grade II and Grade III *(a)*	Grade 0 and Grade I *(n)*	
<59 *(a)*	62	21	83
>90 and 60-89 *(n)*	4	58	62
Total	66	79	145
Sensitivity	Specificity	PPV	NPV
74.7% (CI: 0.68 - 0.78)	93.5% (CI: 0.85 - 0.99)	93.9% (CI: 0.86 - 0.98)	73.4%(CI: 0.67 - 0.77)

Estimated GFR (eGFR) is grouped into stable renal function of more than or equal to 60 mL/min/1.73 m^2 and assigned a negative test (*normal*), less than or equal to 59 mL/min/1.73 m^2 to be on the positive test (*abnormal*).

Grade 0 and I cortical reflectivity are considered normal sign and group II and III to be abnormal finding.

The result shows an ability of the cortical reflectivity to correctly identify those with the compromised renal function (sensitivity) by 74.7% (95%CI: 0.68 - 0.78), specificity of 93.5% (95%CI: 0.85 - 0.99).

The positive predictive value (PPV) was shown to be 93.9% (CI: 0.86 - 0.98) and a negative predictive value (NPV) was 73.4% (CI: 0.67 - 0.77). Positive Likelihood Ratio (LR) of 11.6; with a $p<0.001$ supported our alternative hypothesis.

Renal Cortical Parenchyma Volume

Renal sonographic biometric measurements from 145 participants and the distributions of cortical volumes were as follows:

From the right kidney cortical volumes were; less than 80cc, 75 (51.7%); 81-110cc, 57 (39.3%); and more than 110cc, 13 (9.0%). *table: 4a below*

From the left kidney cortical volumes were; less than 80cc, 67 (46.2%); 81-110cc, 60 (41.4%), and more than 110cc, 18 (12.4%). *table: 4b below.*

These cortical volume categorizations were based on the normal median cortical volume from the normal population which is 88.04 cm^3 for the right kidney and 115.13 cm^3 for the left kidney (33)

Table: 4a. Right kidney cortical volume (n=145)

Cortical Volume	Frequency	Percent %	Valid Percent	Cumulat. Perc.
<80	75	51.7	51.7	51.7
81-110	57	39.3	39.3	91.0
>110	13	9.0	9.0	100.0
Total	145	100.0	100.0	

Table: 4b. Left kidney cortical volume (n=145)

Cortical Volume	Frequency	Percent %	Valid Percent	Cumulat. Perc.
<80	67	46.2	46.2	46.2
81-110	60	41.4	41.4	87.6
>110	18	12.4	12.4	100.0
Total	145	100.0	100.0	

Both tables **4a** and **4b** show right and left cortical volume distribution, almost half of the study population appeared within 46.2-51.7% and their renal cortical volume lies below the normal health adult average.

This study registered 12.4% above normal cortical volume average among CKD patients, this observation can probably have more than one explanation that was not taken care of by this study. However, the noted sonographic finding was larger renal volume among HIV nephropathy individuals which is inversely proportional to CKD renal change caused by other causes.

Table: 5a. Estimated GFR with right kidney cortical volume change (n=145)

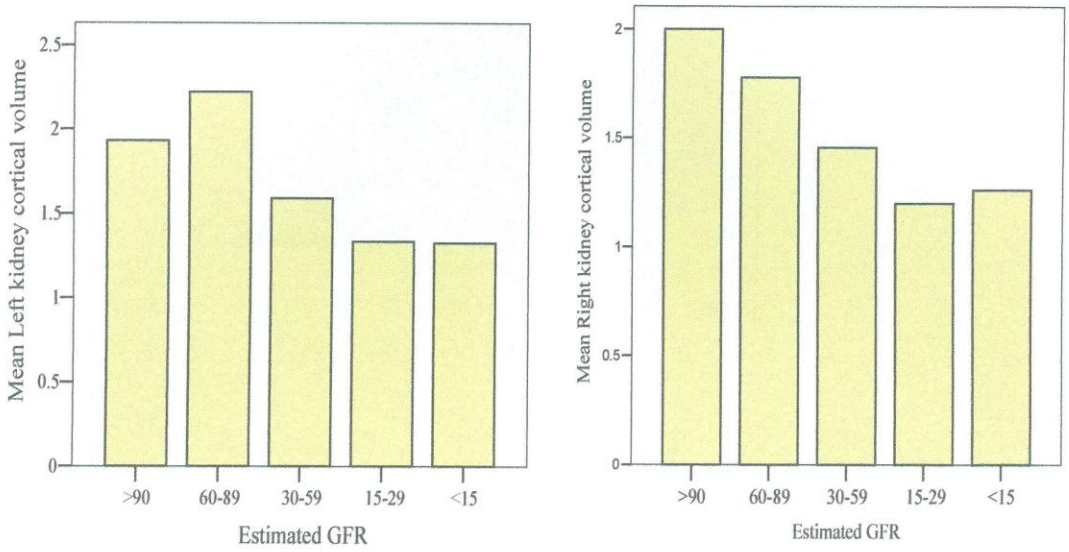
Estimated GFR	Right kidney cortical volume (CC)			Total
ml/min/1.73 m^2	<80cc	81-110cc	>110cc	
>90	8	28	8	44
60-89	4	14	0	18
30-59	14	6	2	22
15-29	13	1	1	15
<15	36	8	2	46
Total	75	57	13	145

Table: 5b. Estimated GFR with left kidney cortical volume change (n=145)

Estimated GFR	Left kidney cortical volume (CC)			Total
ml/min/1.73 m^2	<80cc	81-110cc	>110cc	
>90	7	33	4	44
60-89	2	10	6	18
30-59	11	9	2	22
15-29	12	1	2	15
<15	35	7	4	46
Total	67	60	18	145

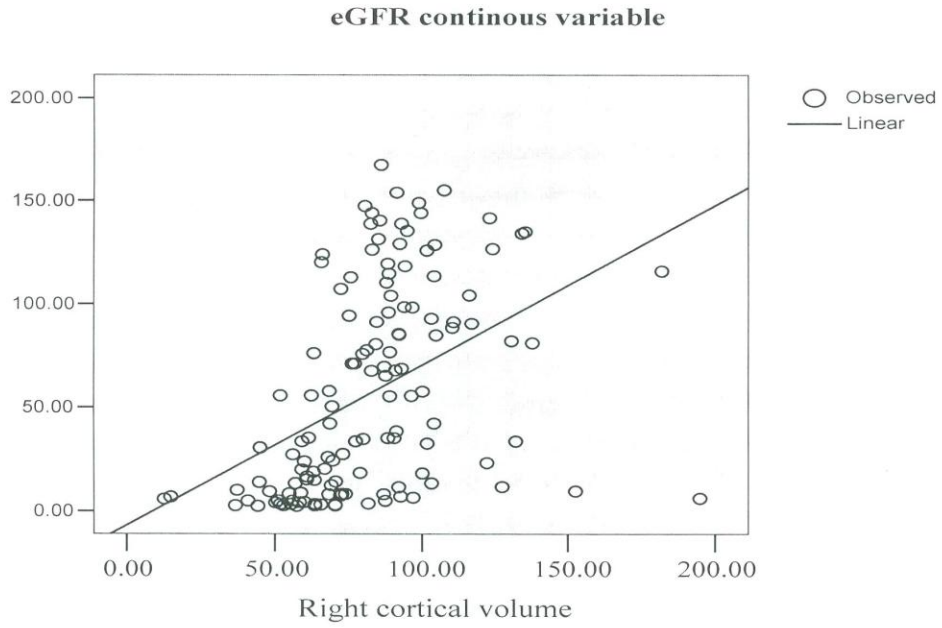
Table 5 shows almost 60% of right and left cortical volumes to be below the normal cortical median volume. Pearson correlation coefficient reveals positive relationship as right and left renal cortical volume and eGFR of ($r \approx +0.49$ ($p < 0.001$); and $r \approx +0.43$ ($p < 0.001$)). Despite significant p-values, Pearson coefficient ranges between +0.7 and +0.3 defining a weak linear association between eGFR and renal cortical volume.

Figure: 5. Right and Left cortical volume with eGFR (n=145)



Linearity is interrupted at different points along the renal function, this visual interpretation corresponds with Pearson correlation coefficient (*$r \approx +0.49$ right kidney and $r \approx +0.43$ for the left kidney*). It concludes that right and left renal cortical volume relates to estimated GFR within the weak coefficient range (*$r = +0.7$ and $+0.3$*).

Figure: 6a: The eGFR and right cortical volume regression correlation

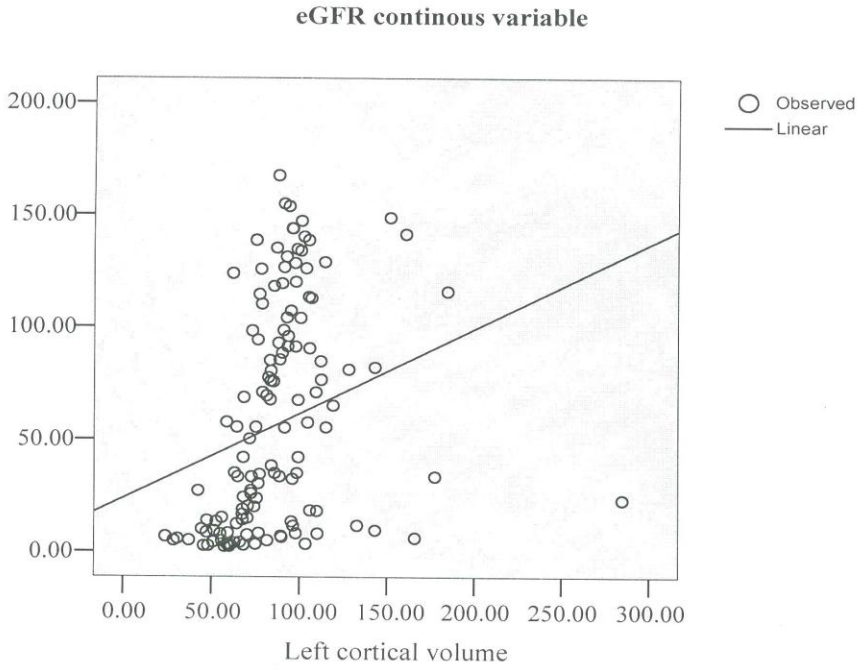


Cortical volume as a predictor of renal function shows the best-fit linear regression line along which the data do not show linearity.

The right cortical volume has shown a weak predictive value for its corresponding renal function as estimated by GFR (r^2=0.184; p<0.001).

Regression line slope confidence interval 95% CI: 0.50-1.04 shows big range of variability if the same study is to be repeated. Hence, requires a bigger sample size.

Figure: 6b: The eGFR and left cortical volume regression correlation



The left renal cortical volume as independent to renal function shows the best-fit linear regression line presenting poor relationship between these two variables.

The left cortical volume has revealed a weak correlation to renal function as estimated by GFR. It is showing a slope **b** (95%CI: 0.16-0.59) and r^2=0.075; p<0.01.

These results do not show credible confirmation to reject the null hypothesis despite its low p-value. The slope confidence interval on other hand shows big variability.

DISCUSSION

Ultrasound technology has advanced the use of this modality beyond the simple display of anatomy, anatomic relationships and localization of lesions. Today, it yields gross anatomic information, imaging the interfaces between tissue structures and reflects the histopathologic characteristics of an organ (50-52).

Ultrasound has been used extensively to build a relationship between cortical echogenicity pattern as sonographic sign to many other variables like renal diseases histopathological pattern (23;25;26;53); renal function variability (23;29) and volume variability (30). On the other hand, the clinical manifestations of patients with CKD including its potential causes and relationship to renal function parameters like creatinine have been well discussed in numerous reports in the literature (54-56)

Despite numerous research findings of renal sonographic changes in relationship to renal function, less attention has been paid to renal sonographic abnormalities in relation to eGFR. Correlating sonographic pathological findings as they relate to renal function (eGFR) has not been well studied. This could be due to the fact that eGFR assessing renal function is demanding and alternatively researchers have concentrated on creatinine despite its non specificity on renal function assessment (1;39).

Renal cortical echogenicity:

At present, a specific tissue characterization by sonography is a field of active research from which these dissertation findings seek to contribute. Our study resembles many (23;28;29), but it has extended the studied knowledge to more specific parameters like using eGFR instead of a non specific creatinine. Despite the extensive work that have been done showing a good work that ultrasound can do, sonologists have not replace the traditional way of assessing renal function using creatinine. Serum creatinine concentration varies with age, sex, muscle mass and diet, and interlaboratory variation between measurements can be as high as 20% (38). One of the barriers to early detection

of CKD is the lack of a precise, cheap, reliable, available and consistent measure of kidney function. This research is therefore an effort to establishing an alternative method. Renal cortical echogenicity strongly relates renal function tested by eGFR, the linearity of these two variables stated above shows ($r \approx +0.79$, $p < 0.001$).

These findings are almost similar to that of Tsau. *et al,* which correlated renal cortical echogenicity and renal function by serum creatinine in pediatric renal diseases ($r = +0.69$, $p < 0.001$) (28). Current research however, reveals a stronger relationship as a Pearson's correlation coefficient increases towards +1. Hricak *et al* in their retrospective study of 109 patients showed a significant correlation between the degree of cortical echogenicity and blood urea nitrogen and creatinine concentrations in support of our current study (23).

Chi. *et al* study concluded that there is a strong relationship between renal parenchymal echogenicity as a predictor of impaired relative renal function. They finally hypothesized that renal echogenicity at renal sonography may help determine which patients require more evaluation of renal function (29). Our study has revealed similar findings to those of Chi *et al* with additional confidence that the current study has used a more reliable measure of renal function (eGFR) and shows stronger relationships.

Like current study, Vergesslich *et al* studied the changes of cortical echogenicity as it correlates with renal function among patient with acute renal failure. They observed that changes in renal function were paralleled with rapid changes in cortical echogenicity. Determined creatinine levels showed a statistically significant correlation with cortical echogenicity grades; $p<0.001$(57). Similar findings were revealed by N'gbesso *et al* who in their study concluded that renal cortical echogenicity increases with the severity of renal insufficiency (58).

The observed linear relationship specifically reveals that kidneys with cortical echogenicity grade I or below usually show renal function of more than 60 mL/min/1.73 m^2, while kidneys with grade II or more present with renal function below 59 mL/min/1.73 m^2. This research however, tested the applicability of cortical echogenicity as a predictor of renal function estimated by GFR. The regression correlation done to quantify the strength of the linear relationship between renal cortical echogenicity as a predictor of renal function, reveals the best fit line with regression correlation coefficient $r^2 = 0.622$, $p<0.001$. At the $p<0.05$ level of significance, there exists enough evidence to conclude that renal cortical echogenicity is useful predictor of renal function (eGFR).

The likelihood that cortical echogenicity can predict renal function among CKD patients was tested using eGFR as a gold standard. Result shows a sensitivity of 74.7% (95% CI: 0.68 - 0.78) identifying the inability of the test to work as a screening tool. However, its specificity of 93.5% (95%CI: 0.85 - 0.99) proves the fact that the test can capture as high as 99% of compromised renal function if the same study is repeated. A Positive predictive Value (PPV) of 93.9% with (95%CI: 0.86 - 0.98) provided the prevalence of CKD is constant, it qualifies the test to be used as a diagnostic tool. Since there is no bilateral difference in sensitivity or specificity from the right and left kidney, the null hypothesis is therefore rejected ($p< 0.001$).

This proves the alternative hypothesis ($r \approx +0.79$, $p < 0.001$) that patient with CKD presenting with cortical echogenicity grade II and above at sonography will be having a compromised kidney function equal to or below 59 mL/min/1.73 m^2. And cortical reflectivity grades I or below will reflect patients of stable renal function. Combining the benefits of sensitivity and specificity, results reveal a positive likelihood ratio (LR+) of +11.6. This is the strongest likelihood ratio which deliberates an increased probability that cortical echogenicity grade II and grade III are good predictor of renal function deterioration

Renal cortical volume

The pathology of chronic kidney disease usually involves structural and functional changes and often interconnected. Regardless of observed renal cortical volume change, this study did not statistically qualify hyperfiltration theorem by Brenner (59). Renal cortical volume change prediction of renal function in our study revealed a likelihood ratio (LR) of less than 4.8 with 95% CI: 0.16-0.59, regression coefficient of $r^2 = 0.075$; in spite of significant p value ($p<0.01$).

Mazzotta *et al* examined healthy adult subjects and nephropathic patients to detect relations between kidney's sonographic dimensions and renal function expressed by creatinine clearance. They concluded that renal parenchymal volume is the more exact sonographic parameter among end-stage renal failure (30). However, the present study did not study the end stage kidney failure but the wide spectrum of renal insufficiency from stable renal function to end stage renal insufficiency. Differences in study design could have shown this inconsistence, end stage kidney disease can be easily appreciated by signs and symptoms of the patient. This research investigated benefits of sonographic picked renal cortical volume to detect renal function across the whole spectrum of CKD patients advocating on early intervention.

Burkhardt *et al* observed that ultrasonography cannot replace or complement eGFR in order to detect early reduced renal function in the elderly age (36). The aim of Burkhardt research was to prove a new method to a routine sonography for renal cortical volume assessment to demonstrate renal function. The current study has indicated the similar findings as that of Burkhardt *et al*; however, these two studies differ in the type of population studied and renal function stage considered. With these reasons we can conclude our findings based on Burkhardt research with precaution.

Troell *et al* looked into the relationship that might exist between ultrasonographically calculated renal parenchymal volume and kidney function. They found a high correlation between renal parenchymal volume and GFR and concluded that ultrasonographic determination of renal parenchymal volume is a reliable method to evaluate glomerular filtration rate in children with recurrent urinary tract infections (37).

These findings differ to current study which showed a weak correlation between cortical volume and renal function $r \approx +0.49$. These differences could be explained by different situations that, Troell observation based only in children with enlarged kidneys different from ours that recruited adult with expected shrunken kidneys. On the other hand, differences from the current study could have been contributed from different diseases being studded and negative volume change caused by CKD rather than positive volume change caused by recurrent ascending urinary tract infection.

There could be a strong correlation on positive cortical volume change (renal expansion) rather than negative cortical volume change (renal shrinkage) as shown by these studies if patients' age is standardized. Vergesslich *et al* studied acute renal failure patients who showed a positive renal cortical volume change and concluded that changes in renal function are parallel with rapid positive changes in renal size (57).

The current research dealing with comparing biometrical sonographic cortical volume change as a predictor of renal function estimated by GFR, lacks supporting similar literature to verify its importance. This has been observed from literature search which showed the relationship between cortical volume and creatinine, also dealing more with children and other diseases rather than CKD. This observation therefore, creates an opportunity for more researchers to work more on this area, bearing in mind that metabolic diseases are on the alarming increase which predispose patients to chronic kidney disease especially CKD.

If the recommended gold standard for estimating renal function is eGFR and practitioners look at it as a time consuming task, a dedicated research to validate renal cortical volume as predictor of eGFR can be of urgency. Since ultrasound is done by a separate dedicated department and its findings are reproducible, can be easily provided to Physicians or Nephrologist for betterment of our patients.

Limitations of the Study

Ultrasound is a highly user dependent procedure from which comparison of organs echogenicity, renal biometric measurements and interpretations done by a newly introduced beginner like residents, might have introduced some findings and reporting error from the research results.

Some of patients recruited were stable but on anti failures, these probably could have their liver reflectivity changed due to pre morbid heart failure that might have contributed to false right renal cortical echogenicity interpretation.

It was expected that diffuse renal parenchyma disease would cause progressive reduction in cortical renal volume. This was contrary for HIV nephropathy kidneys which could have changed the pattern of volume change among CKD patients and yield a false interrelationship between renal cortical change and its function.

The MDRD equation for determining eGFR uses serum albumin as one of the variables, but to patients with CKD low serum albumin it can be attributed not only due to kidney disease but also failure of protein intake as the sick may lose appetite to eat or as bread winner cannot get enough protein without working. This might have miscalculated the gold standard dependent variable (eGFR).

CONCLUSION

Correlations between renal cortical echogenicity, structural parameters (*renal cortical parenchyma volume change*) and renal function estimated by GFR suggest that renal cortical echogenicity sign may potentially be useful as a surrogate marker of the renal function, (LR) of +11.6 and $p<0.001$. To be more precise, cortical echogenicity grade I or below will usually manifest renal function of more than 60 mL/min/1.73 m^2 and renal function of less than 59 mL/min/1.73 m^2 manifest cortical echogenicity grade II or more.

However, this study found unfavorable regression coefficient of $r^2 = 0.075$, 95% CI: 0.16-0.59 associated with (LR) of less than 4.8, hence did not qualify our alternative hypothesis. At present, a precise prediction of renal function based on renal cortical volume change requires a big sample size since its confidence interval comes with high prediction variability.

RECOMMENDATIONS

It is recommended that research be undertaken to identify alternative accurate and cost effective methods of measuring kidney function, especially in patients with eGFR <59 mL/min/1.73m^2 among the two, renal cortical echogenicity and renal cortical volume.

Protocol should be in place to assist early identification of people registering for routine ultrasound of any indication, who might be at risk of CKD on the basis of increased renal cortical echogenicity. That means any patient with cortical echogenicity grade two or more should be referred for renal evaluation.

Capacity building to sonographers is needed to proper cortical echogenicity grades interpretation. This intervention is to optimize early diagnosis and reducing disease progression among patients with CKD

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