

CORRELATION OF MEAN VALUES OF SERUM CREATININE BASED ON ECHOGENICITY OF KIDNEYS ON RENAL ULTRASOUND

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ABSTRACT

OBJECTIVE: To determine the mean values of serum creatinine based on echogenicity of kidneys on renal ultrasound. **MATERIALS AND METHODS:** A total of 120 selected patients of nephrology fulfilling the inclusion criteria were selected and referred to radiology department for ultrasound abdomen or KUB. All renal ultrasounds were done by real time gray scale ultrasound. Ultrasound of the liver/spleen was performed simultaneously in comparison with kidneys in order to determine grades of renal parenchymal disease. Liver and spleen echogenicity must be normal for valid comparison. In vitro estimation of serum creatinine was done. Information of each patient was collected through a predesigned proforma (attached herewith). The results were analyzed by SPSS software by descriptive and inferential statistics. **DESIGN:** Descriptive cross sectional. **RESULTS:** The average age of the patients was 33.3 – 12.57 years. The mean serum creatinine was 2.82 – 1.69 mg/dl for Grade 1, 3.87 – 2.08 mg/dl for Grade 2, 3.95 – 1.58 mg/dl for Grade 3, and 7.52 mg/dl for Grade 4. Mean serum creatinine was significant among grade. **CONCLUSION:** It is concluded that renal echogenicity is a better parameter than serum creatinine for estimating renal function in CKD and has the added advantage of irreversibility.

Key Words: Chronic Kidney Disease, Serum creatinine, Renal ultrasound, Echogenicity

Introduction

Chronic Kidney Disease is a major health problem and one of most common causes of renal failure.^{1,2} Its incidence and prevalence is increasing day by day, perhaps as a consequence of diabetes mellitus, hypertension and obesity.^{2,10} CKD generally remains asymptomatic until stage 4, so most patients are identified because of routine blood/urine tests or ultrasound.¹⁰

It involves progressive loss of function and structure of kidneys over many years. Renal dysfunction can be diagnosed by pathological abnormalities, changes in renal function markers e.g urea/ creatinine or by renal ultrasound. On ultrasound small shrunken kidneys with thin echogenic cortex or parenchyma indicates chronic kidney disease with irreversible damage.¹

Serum creatinine level is an endogenous serum marker made by breakdown of body muscle protein.^{1,2} Creatinine can also be measured in urine and saliva as alternative noninvasive methods.^{1,11} A rise in serum creatinine concentration of at least 0.3mg/dl indicates acute kidney damage.⁵ It is most commonly used method to determine renal function in clinical practice.³ However isolated serum creatinine is unable to diagnose renal parenchymal disease, as serum creatinine is affected by certain factors e.g. age, race, gender, diet, muscle mass.^{2,3} Serum creatinine can estimate change in GFR but not the absolute GFR, so may lead to misdiagnosis of CKD.^{7,10} Ultrasound is an ideal modality to determine renal parenchymal disease because of its noninvasiveness,

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easy availability, reliability, affordability and visualization of kidneys.^{1,5} Renal ultrasound is still most appropriate method for imaging renal failure and should be combined with other labs to assess the progression of CKD.^{1,4} Renal echogenicity and its grading correlates better with serum creatinine than other sonographic parameters.¹ Echogenicity refers how bright or dark something appears in the grey scale imaging. Kidney appears isoechoic (equal in brightness) or hypoechoic (darker) when compared with normal liver or normal spleen.⁶ CKD is typically associated with increased echogenicity.^{1,6} Although renal disorders may present without changes in echogenicity, but if increased parenchymal echogenicity is noted it is usually abnormal.^{6,8} Increased echogenicity was reported to have 96% specificity and 67% PPV (positive predictive value) for the presence of parenchymal kidney disease.⁶

The purpose of our study is to demonstrate the adjuvant role of ultrasound in making diagnostic and prognostic decisions regarding CKD. The findings if correctly interpreted are accurate enough to be used as indirect measure of lab values of serum creatinine. This study hence can help us in early detection of renal parenchymal disease by ultrasound so that patients are not neglected or remain undiagnosed. This study is new in our region and will add to the already existing literature.

Material and Methods

All indoor and outdoor patients of nephrology / medicine fulfilling the inclusion criteria (Patients (of all 4 grades) above the age of 12 yrs were included regardless of gender with CKD \geq 6 months duration having GFR $<$ 90 ml/n) were taken from KRL Hospital for ultrasound abdomen or KUB. Before each examination the procedure was explained to the patient and informed consent was taken by them. Study was conducted after approval from hospital ethical committee. Ultrasonography was conducted by researcher herself.

All renal ultrasounds were done by real time gray scale ultrasound performed by a consultant radiologist having at least three years of experience (Volusion GE PRO V 730), using 3.5 MHz curvilinear probe in supine and decubitus position with deep inspiration.

Ultrasound of the liver/spleen was performed simultaneously in comparison with kidneys to determine grades of renal parenchymal disease. The result was correlated by serum creatinine. Information of each patient was collected through a predesigned proforma. The collected data was analyzed by SPSS version 17. Results were calculated by descriptive and inferential statistics.

Results

A total of (n=120) selected patients of nephrology and medicine fulfilling the inclusion criteria were selected for ultrasound abdomen or KUB. Age distribution of the patients is presented in (Fig.1) while age statistics in (Tab.1).

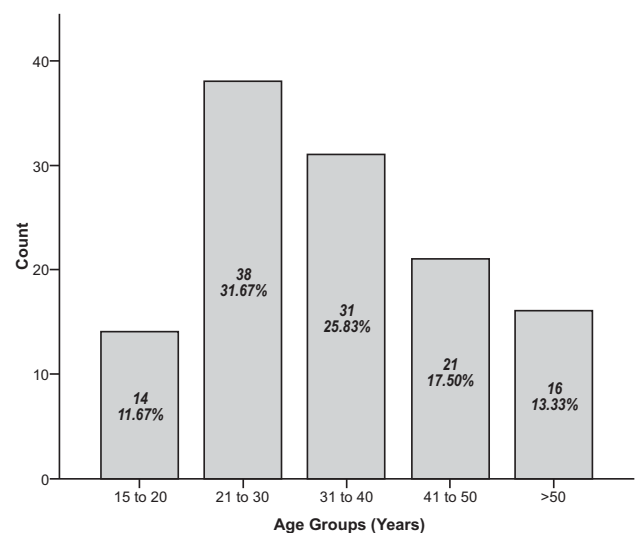


Figure 1: Age distribution of the patients n=120

STATISTICS		AGE(YEARS)
Mean		33.33
95% Confidence Interval for Mean	Lower Bound	31.05
	Upper Bound	35.60
Median		28.50
Std. Deviation		12.57
Minimum		15
Maximum		60
Inter quartile Range		18

Table 1: Age statistics of the patients

Overall mean serum creatinine was 4.54 – 2.68 mg/dl while the mean serum creatinine was 2.82 – 1.69 mg/dl for Grade 1, 3.87 – 2.08 mg/dl for Grade 2, 3.95 – 1.58 mg/dl for Grade 3, and 7.52 mg/dl for Grade 4. Mean serum creatinine was significant among grade as shown in (Tab.2).

Stratification analysis according to age groups (= 40 years and >40 years) were performed to estimated mean serum creatinine as presented in (Tab.3&4) respectively.

Grade of Echogenicity	Serum Creatinine (mg/dl)						F-Value	P-Value
	N	Mean	SD	95% CI for Mean	Min	Max		
Grade 1	30	2.82	1.69	2.19-3.45	0.94	9.10	30.92	0.0005
Grade 2	30	3.87	2.08	3.09-4.65	1.30	10.40		
Grade 3	30	3.95	1.58	3.36-4.54	1.20	6.50		
Grade 4	30	7.52	2.59	6.55-8.48	3.20	11.52		
Total	120	4.54	2.68	4.05-5.02	0.94	11.52		

CI: Confidence Interval; SD: Standard Deviation, Min: Minimum, Max: Maximum, ANOVA test applied

Table 2: Mean values of serum creatinine based on echogenicity of kidneys on renal ultrasound

Grade of Echogenicity	Serum Creatinine (mg/dl)						F-Value	P-Value
	N	Mean	SD	95% CI for Mean	Min	Max		
Grade 1	28	2.76	1.72	2.10-3.43	0.94	9.10	20.15	0.0005
Grade 2	22	3.20	1.15	2.68-3.71	1.30	4.90		
Grade 3	21	4.05	1.59	3.33-4.77	1.20	6.50		
Grade 4	12	7.30	2.78	5.54-9.07	3.50	11.52		
Total	83	3.86	2.29	3.36-4.36	0.94	11.52		

CI: Confidence Interval; SD: Standard Deviation, Min: Minimum, Max: Maximum ANOVA test applied after stratified of age groups (≤40 years)

Table 3: Mean values of serum creatinine based on echogenicity of kidneys on renal ultrasound for the patients of age below and equal to 40 years

Grade of Echogenicity	Serum Creatinine (mg/dl)						F-Value	P-Value
	N	Mean	SD	95% CI for Mean	Min	Max		
Grade 1	2	3.55	1.34	-8.52-15.62	2.60	4.50	6.31	0.002
Grade 2	8	5.73	2.92	3.29-8.16	3.50	10.40		
Grade 3	9	3.71	1.62	2.47-4.95	1.80	6.50		
Grade 4	18	7.66	2.52	6.41-8.92	3.20	11.00		
Total	37	6.06	2.89	5.10-7.02	1.80	11.00		

CI= Confidence Interval; SD= Standard Deviation ANOVA test applied after stratified of age groups (>40 years)

Table 4: Mean values of serum creatinine based on echogenicity of kidneys on renal ultrasound for the patients of age above 40 years

Discussion

Creatinine is a waste product of metabolism that is primarily excreted by kidneys. Virtually all the creatinine that is filtered at the glomerulus is excreted without reabsorption in the tubules and so its level in the blood is used as an index to renal function.¹² The normal range of serum creatinine is 0.6 - 1.5 mg/dL and salivary creatinine is 0.05 - 0.2 mg/dL.¹²

Ultrasonography is the first, and in most cases the only imaging investigation required in the workup of chronic renal failure. Observation of a small kidney with a thin, echogenic cortex or parenchyma indicates irreversible damage.^{13,14} The best screening modality to evaluate renal insufficiency in patients is sonography.¹⁵ As ultrasonographic findings like echogenicity, longitudinal length, parenchymal, and cortical thickness represent irreversible changes, ultrasonography is a better imaging modality when it comes to ascertaining the progression of the disease.^{13,14} Small size and increased parenchymal echogenicity are directly correlated with progression of disease.¹⁵

Similar result was also observed in a randomized controlled trial published in Journal of Clinical Imaging Science in 2013. In this study out of 60 selected patients 48.3% had Grade 1 CKD, 35% had Grade 2 CKD, 11.7% had Grade 3 CKD, 5% had Grade 4 CKD. The mean serum creatinine was 2.80 mg/dl for Grade 1 (range: 0.9-9.2 mg/dl), 3.69 mg/dl for Grade 2 (range: 1.2-10.3 mg/dl), 3.86 mg/dl for Grade 3 (range: 1.1-6.5 mg/dl), and 7.90 mg/dl for Grade 4 (range: 3.1-11.4 mg/dl).¹

Our study showed statistically significant positive correlations between serum creatinine and renal echogenicity grading (0.0005) from Grade 1 to Grade 4 CKD. A study by Moghazi et al., showed that renal echogenicity has the strongest correlation with histologic parameters (glomerular sclerosis, tubular atrophy, interstitial fibrosis, and interstitial inflammation).¹⁶ Research by Pivnsalo et al., showed that a highly echogenic cortex was the most common abnormality; this was slightly more frequent in tubulointerstitial disease (75%) than in glomerular disease (61%).¹⁷ In a previous study, Hricak et al., showed a statistically significant positive correlation between cortical echogenicity and the severity of glomerular sclerosis, focal tubular atrophy, the number

of hyaline casts per glomerulus, and focal leukocytic infiltration.¹⁸

Creatinine is a large molecule, with high molecular weight (MW 113Da and molecular radius of 3.2 Å) maintained at constant plasma levels by kidneys. They also exhibit low lipid solubility. Thus, in a healthy state under normal conditions owing to its physical properties it is unable to diffuse easily across the cells and the tight intercellular junction of the salivary gland.^{19,20} But in the diseased state possibly there is an alteration in the permeability of the salivary gland cells.²¹ Also the increased serum creatinine levels in CKD patients create a concentration gradient that facilitates increased diffusion of creatinine from serum in to saliva.^{22,23} The normal range of serum creatinine is 0.6-1.5 mg/dL and salivary creatinine is 0.05-0.2 mg/dL.²⁴

Few studies have shown a positive correlation between the serum and salivary creatinine concentration hence it can also be used as an adjunct in the progression of renal parenchymal disease. Some other studies have established a very strong correlation between the estimated e GFR as a predictor of renal function with the sonographic characteristics especially the size echogenicity and the corticomedullary differentiation, and furthermore it can also serve as a tool for follow up.^{25,26} These sonographic parameters serve as an important parameter in preemptive predictor for renal insufficiency.²⁷

Moreover ultrasound is freely available, completely non-invasive and economical hence it can be used as a very good alternate method for renal status assessment especially in those patients who are high risk.^{28,29}

Conclusion


We conclude from our study that renal echogenicity and its grading correlates better with serum creatinine in CKD. Renal echogenicity is a better parameter than serum creatinine for estimating renal function in CKD and has the added advantage of irreversibility.

Conflict of Interest: None

References

1. Siddapa JK, Singla S, Al Ameen M, Rakhshith SC, Kumar N. Correlation of ultrasonographic parameters with serum creatinine in chronic kidney disease. *J Clin Imaging Science*. 2013; **3**: 28.
2. Ghasemi A, Azimzadeh I, Zahediasl S, Azizi F. Reference values for serum creatinine with jaffe compensated assay in adult Iranian subjects: Tehran lipid and glucose study. *Arch Iran Med*. 2014; **17(6)**: 394-9.
3. Araujo NC, Rioja Lda S, Rebelo MA. A clinical predictor index for renal survival. *J Bras Nephrol*. 2010; **32(1)**: 27-3.
4. 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; **74(1)**: 46-52.
5. Licurse A, Kim MC, Dziura J, Forman HP, Formica RN, Makarov DV, et al. Renal ultrasonography in the evaluation of Acute kidney injury: developing a risk stratification framework. *Arch intern Med*. 2010; **170(21)**: 1900-07.
6. Faubel S, Patel NU, Lockhart ME, Cadnapaphornchai MA. Renal relevant radiology: Use of ultrasonography in patients with AKI. *Clin J Am Nephrol* 2014; **9(2)**: 382-94.
7. Inker LA, Schmid CH, Tighiouart H, Eckfeldt JH, Feldman HI, Greene T, et al. Estimating glomerular filtration rate from serum creatinine and cystatin C. *N Engl J Med*. 2012; **367(1)**: 20-9.
8. Daneman A, Navarro OM, Somers GR, Mohanta A, Jarrin JR, Traubici J. Renal pyramids: Focused sonography of normal and pathological processes. *Radiographics*. 2010; **30(5)**: 1287-307.
9. Jessai S, Bux R, Jafar TH. Prevalence, determinants and management of chronic kidney disease in Karachi, Pakistan- a community based cross sectional study. *BMC Nephrol*. 2014; **15(1)**: 90.

10. Methven S , MacGregor MS. Clinical management of chronic kidney disease. *Clinical medicine*. 2009; **9(3)**: 269-72.
11. Venkatapathy R, Govindarajan V, Oza N, Parameswaran S, pennagaram Dhanasekaram B, Prashad KV. Salivary creatinine estimation as an alternative to serum creatinine in chronic kidney disease patients. *Int J Nephrol*. 2014: 6.
12. C. Streckfus and L. Bigler, The use of soluble, salivary c-erbB-2 for the detection and post-operative follow-up of breast cancer in women: the results of a five-year translational research study, *Advances in Dental Research* 2005; **18(1)**: 17-24.
13. O Neill WC. Chronic renal failure. In: O Neill WC, editor. *Atlas of renal ultrasonography*. Philadelphia: W.B. Saunders Company; 2001. p. 41-3.
14. O Neill WC. Sonographic evaluation of renal failure. *Am J Kidney Dis* 2000; **35**: 1021-38.
15. Khati NJ, Hill MC, Kimmel PL. The role of ultrasound in renal insufficiency: The essentials. *Ultrasound Q* 2005; **21**: 227-44.
16. Moghazi S, Jones E, Schroeppele J, Arya K, McClellan W, Hennigar RA, et al. Correlation of renal histopathology with sonographic findings. *Kidney Int* 2005; **67**: 1515-20.
17. Pivnsalo M, Huttunen K, Suramo I. Ultrasonographic findings in renal parenchymal diseases. *Scand J Urol Nephrol* 1985; **19**: 119-23.
18. Hricak H, Cruz C, Romanski R, Uniewski MH, Levin NW, Madrazo BL, et al. Renal parenchymal disease: Sonographic-histologic correlation. *Radiology* 1982; **144**: 141-7.
19. Chiou WL and Pu FS. Creatinine. VIII: saliva levels of endogenous true creatinine in normal subjects, *Clini Pharmacol and Therapeut*. 1979; **25**: 777-82.
20. Martin K and Burgen AS. Changes in the permeability of the salivary gland caused by sympathetic stimulation and by catecholamines. *General Physiol*. 1962; **46**: 225-43.
21. Ivanovski K, Naumovski V, Kostadinova M, Pesevska S, Drijanska K, and Filipce V. Xerostomia and salivary levels of glucose and urea in patients with diabetes. *Prilozi*. 2012; **33**: 219-29.
22. Obuchowski NA, Receiver operating characteristic curves and their use in radiology. *Radiology*. 2003; **229**: 3-8.
23. Nakahari T, Yoshida H, and Imai Y. Transepithelial fluid shift generated by osmolarity gradients in unstimulated perfused rat submandibular glands. *Experimental Physio*. 1996; **81**: 767-79.
24. C. Streckfus and L. Bigler, The use of soluble, salivary c-erbB-2 for the detection and post-operative follow-up of breast cancer in women: the results of a five-year translational research study, *Advances in Dental Research* 2005; **18(1)**: pp. 17-24.
25. Yaprak M, 'akir , Turan MN, Dayanan R, Akin S, Degirmen E, Yildirim M, Turgut F. Role of ultrasonographic chronic kidney disease score in the assessment of chronic kidney disease. *International urology and nephrology*. Jan 2017; **49(1)**: 123-31
26. Korkmaz M, Aras B, G neyli S, Yilmaz M. Clinical significance of renal cortical thickness in patients with chronic kidney disease. *Ultrasonography*. Jan 2018; **37(1)**: 50.
27. Megally HI, Mohamed MZ, Mohamed WH, Mohamed MA. Renal cortical thickness as an indicator of renal insufficiency in chronic kidney disease. *Journal of Current Medical Research and Practice*. Jul 2020; **5(3)**: 268.
28. Mansoor A, Ramzan A, Chaudhary AN. Determination of best grey-scale ultrasonography parameter for assessment of renal function in chronic kidney disease. *Annals of PIMS ISSN*. 2016; **1815**: 2287.

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29. Devkota K, Gupta MK, Pant AR, Kark P. Correlation of Duplex Ultrasonographic Parameters with Glomerular Filtration Rate in Chronic Kidney Disease. *Journal of Nepal Health Research Council*. Aug 2019; **17(1)**: 32-7.