DOI: https://doi.org/10.53350/pjmhs211572072

ORIGINAL ARTICLE

Serum Serum Cystatin C vs Creatinine (SCr) as early marker of acute renal dysfunction- A comparative study

ARAFAT AHMAD[1], USAMA BIN GHAFFAR[2], SANKET DADARAO HIWARE[3], MOHAMMED TAHER ALI[4], SAMINA WASI[5]
[1]Assistant Professor, Department of Biochemistry, College of Medicine Imam Abdulrahman Bin Faisal University, Dammam, Saudi Arabia. Email: aahmad@iau.edu.sa
[2]Assistant professor, Department of Pathology, College of medicine, Majmaah University, Al Majma'ah, Saudi Arabia. Email: ubghaffar@gmail.com
[3]Assistant professor, Department of Anatomy, College of Medicine, Imam Abdulrahman Bin Faisal University, Dammam, Saudi Arabia. Email: sdhiware@iau.edu.sa (corresponding author)
[4]Associate professor, Department of Pharmacology, College of Clinical pharmacy, Imam Abdulrahman Bin Faisal University, Dammam, Saudi Arabia. Email: mtali@iau.edu.sa
[5]Assistant Professor, Department of Biochemistry, College of Medicine, Imam Abdulrahman Bin Faisal University, Dammam, Saudi Arabia. Email: Skiasi@iau.edu.sa
Corresponding Author: Dr. Sanket Dadarao Hiware, Assistant professor, Department of Anatomy, College of Medicine, Imam Abdulrahman Bin Faisal University, Email: sdhiware@iau.edu.sa

ABSTRACT

Aim: To compare serum creatinine (SCr) and serum cystatin C as early marker of acute kidney dysfunction.
Methodology: The present cross sectional observation study consisted of eighty- four ICU admitted patients (critical ill). A randomization of patients into 2 groups was done. Patients with normal kidney functions were put in group 1 while those with impaired kidney functions were in group 2. The estimation of serum creatinine (SCr) and serum cystatin C was done. Mann Whitney U and ch- square test was used for statistical inference.
Results: In group 1 patients, mean serum creatinine (SCr) was 0.30± 0.21 mg/dl and in group 2 was 0.56±0.41 mg/dl. Serum cystatin C level in group 1patients found to be 0.42±0.17 mg/l and 1.5±0.68 mg/l in group 2 patients. Accuracy for Cys- C was better than SCr (90% vs 67%). Specificity for SCr was 97% whereas for Cys- C was 95%. Sensitivity for Cys-C was 80% while for SCr was 25%. SCr had PPV of 92% and NPV of 61% and for Cys- C it was 93% and 83% respectively.
Conclusion: Serum cystatin C found to be better than serum creatinine for the identification of impairment of kidney functions in critically ill patients. Hence, assessment of Cys-C is of great concern in AKI.
Key words: Acute renal failure, serum creatinine, serum, renal impairment

INTRODUCTION

Acute renal injury refers to frequent reduction in glomerular filtration rate (GFR). Impaired kidney function is commonly encountered complication in critically ill patients in ICU.[1] GFR is regarded as indicator for normal renal function.[2] GFR measurement is done with insulin clearance.[3] But it is not possible to obtain and claim constant rate infusions and moreover it is not easy to measure precisely. GFR is also measured through serum creatinine concentration.[4] When GFR level decreases about 40 ml/min/1.73 m^2, the level of serum creatinine starts rising. Serum creatinine level is considered important indicator for renal function monitoring.[5]

Parameters like age, sex, mass of muscles, ingestion of proteins and drugs can affect serum creatinine (SCr) resulting to an imprecise valuation of renal impairment.[6] It is eident in literature that subjects with altered level of GFR may have normal SCr.[7] It is also observed that acute changes in renal function may pose difficulty in assessment of GFR especially in serious patients.[8]

Serum cystatin C is a cystatin protease inhibitor, non-glycosylated protein. It has potential role in assessment of GFR in place of creatinine. Its production is continuous by all cells of body.[9] Serum cystatin C offers benefit that unlike serum creatinine (SCr), age, race, sex, ingestion of protein, mass of muscles, infectious as well as inflammatory diseases and liver diseases does not affect it.[10] Its level starts rising when the concentration of GFR decreases. It may be considered comparable to serum creatinine (SCr) in assessing acute kidney changes.[11] Considering this, we attempted present study to compared serum creatinine (SCr) and serum cystatin C as early marker of acute renal dysfunction.

METHODOLOGY

The present prospective cross sectional single centre study was started with the approval from ethical review and clearance committee. A total of eighty- four critical ill patients admitted to ICU were recruited. Family members or relatives of patients were agreed to be the part of the study with consent obtained on paper. Patients with thyroid, kidney impairment and those requiring kidney replacement considered excluded.

Based on estimation of GFR, a randomization of patients into 2 groups was done. Patients with normal renal function were kept in group 1 and those with altered renal function were kept in group 2. Patients were kept non-urinated for at-least 24-hours. Following this, urine sample was obtain to measure the creatinine clearance (CrCl) as: CrCl (ml/min) ¼ (urine volume X urine creatinine)/ (SCr X1440). With the value of CrCl we estimated GFR (eGFR). A 5 ml of venous blood was aspirated in a test tube, centrifuged and supernatant was separated for serum creatinine (SCr) and serum cystatin C level measurement. Particle-enhanced immunonephelometric assay with the N latex cys-C assay kit was used for Serum cys-C measurement. eGFR value < 80 ml/min/1.73 m^2 was suggestive of kidney dysfunction.

Statistical analysis: We used SPSS version 20.0 and the chi- square and Mann Whitney U test compared different variables with p <0.05 indicated level of significance.

RESULTS

Table 1 Demographic parameters of patients

Parameters	Value
Mean age	52.4 years
Gender, Male: Female	50:34
Length of ICU stay	9.2 days
Number of patients on mechanical ventilation	45

We observed 52.4 years as mean age. Male: Female ratio was 50:34. The mean length of ICU stay was 9.2 days and number of patients on mechanical ventilation were 45.

Table 2 Clinical diagnosis of patients

Diagnosis	Number	P value
Multiple trauma	24 (28.5%)	<0.05
Pulmonary disease	15(17.8%)	
Neurological disease	7(8.3%)	
Sepsis	17(20.2%)	
Cardiological disease	13 (15.4%)	
Intoxication	4 (4.7%)	
Hematologic-oncologic disease	3 (3.5%)	
Metabolic disease	1(1.1%)	

Mann Whitney U test, Significance, <0.05

Clinical diagnosis of patients was multiple trauma in 24, pulmonary diseases in 15, neurological diseases in 7, sepsis in 17, cardiological diseases in 13, intoxication in 4, Hematologic-oncologic diseases in 3 and metabolic disease in 1 patient. The difference was significant (P< 0.05) (Table 2, Graph 1).

Graph 1

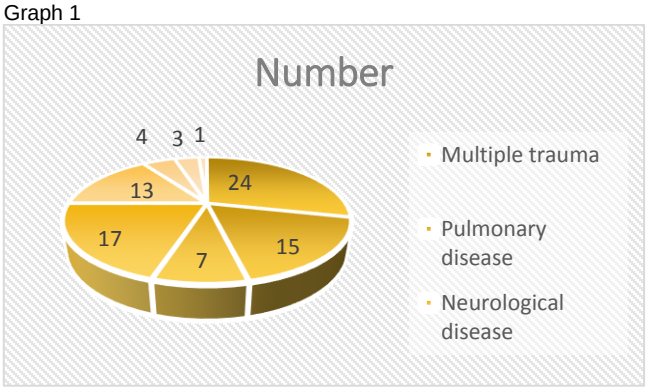

Table 3 Comparison of serum creatinine (SCr) and serum cystatin C

Parameters	Group 1	Group 2	P value
Serum creatinine (SCr)	0.30± 0.21	0.56±0.41	<0.05
Serum cystatin C	0.42±0.17	1.5±0.68	<0.05

Mann Whitney U test, Significance, <0.05

Group 1 patients exhibited 0.30± 0.21 mg/dl and group 2 patients exhibited 0.56±0.41 mg/dl of mean serum creatinine (SCr). Group 1 patients showed 0.42±0.17 mg/l and group II 1.5±0.68 mg/l of serum cystatin C level which was statistically significant (P< 0.05) (Table 3, Graph 2).

Graph 2

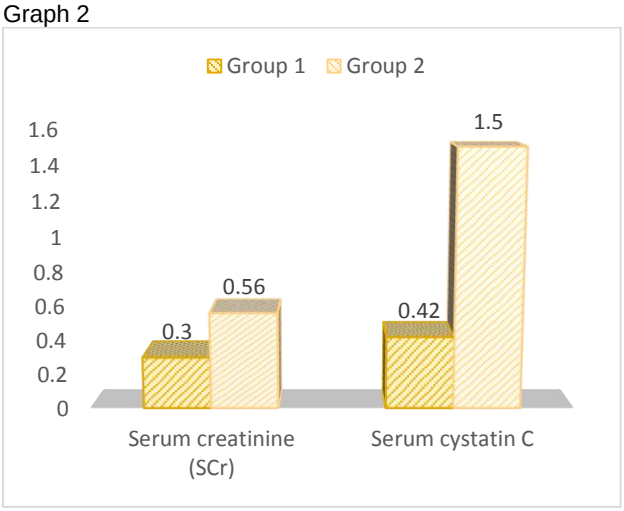

Table 4 Assessment of predictive value of SCr and cys-C in relation to eGFR

		Normal	Reduced	Predictive value
SCr	Normal	52	21	Sensitivity- 25%
				Specificity- 97%
				Accuracy- 67%
	Elevated	2	9	PPV- 92%
				NPV- 61%
Cys-C	Normal	51	8	Sensitivity- 80%
				Specificity- 95%
				Accuracy- 90%
	Elevated	3	22	PPV- 93%
				NPV- 83%

Chi- Square test, Significance, <0.05

Accuracy for Cys- C was better than SCr (90% vs 67%). Specificity for SCr was 97% whereas for Cys- C was 95%. Sensitivity for Cys-C was 80% while for SCr was 25%. SCr had PPV of 92% and NPV of 61% and for Cys- C it was 93% and 83% respectively.

DISCUSSION

We conducted present study to compare serum creatinine (SCr) and serum cystatin C as early marker of acute kidney function. Impaired renal function is one of the biggest complications in critically ill patients inspite of recent development in diagnostic criteria.[12] Based on muscle mass and dietary habits, the production of creatinine changes significantly. Renal tubules secrete creatinine.[13] Out of total creatinine secretion in the body, renal tubules contribute 20% and subsequently decrease in GFR. Studies have shown that >0.3 mg/dL or higher level of serum creatinine are independently linked with prolonged hospital stay.[14,15] That's why GFR may be correctly determined with serum creatinine. It is also considered insensitive and nonspecific parameter for renal function assessment.[16] Serum creatinine has half- life of approximately 4 hours. Cystatin C formation and liberation is not affected by kidney conditions. This makes it most suitable GFR marker. Its half- life is for 1.5- 2 hours only. sCyC is now considered better than sCr for assessment of early GFR changes and as a marker of kidney injury.

Moreover, routine laboratory measurement is readily increasing.[17]

Our study included 84 (50 males and 34 females) critically ill ICU admitted patients who showed signs of renal failure. It was observed that 52.4 years was mean age in patients. 9.2 days were mean length of ICU stay and 45 patients were on mechanical ventilation. Che et al[18] conducted a study among 628 patients selected for cardiac surgery. In all, sCyC and sCr were measured at baseline, 24 hours and 48 hours following surgery. 178 patients (28.3%) showed CSA-AKIsCr development. Results of the study demonstrated that 42 patients (6.8%) had MAEs. 228 patients (36.3%) showed ≥30% rise in level of sCyC in 2 days after surgery.

Ours results further revealed that 24 (28.5%) patients were diagnosed for multiple trauma, 15(17.8%) with pulmonary diseases, 7(8.3%) with neurological diseases, 17(20.2%) with sepsis, 13 (15.4%) with cardiological diseases, 4 (4.7%) with intoxication, 3 (3.5%) with hematologic-oncologic diseases and 1(1.1%) with metabolic diseases. Murty et al[19] conducted a study on 200 healthy participants and 130 patients having acute renal injury. It was found that 56.2% of patients in early phase had normal serum creatinine levels, while all patients had raised serum cystatin C. It was observed that parameters such as age, gender, muscle mass, and ethnicity did not affect serum cystatin C level and in early stages of AKI, it depicted renal function more accurately.

Our results demonstrated that the mean serum creatinine (SCr) level was 0.30± 0.21 mg/dl in group 1 patients and 0.56±0.41 mg/dl in group 2 patients. Serum cystatin C level was 0.42±0.17 mg/l in group 1 and 1.5±0.68 mg/l in group 2 patients. Asilioglu et al[20] determined serum cystatin C (cys-C) level in seriously diseased child patients suffering AKI. It was revealed in the study that there was correlation between the inverse of serum cys-C and eGFR which found to be better than the correlation between the inverse of SCr and eGFR. Kidney function impairment was correctly and effectively determined by serum cys-C in comparison to SCr.

The results of our study depicted higher accuracy of Cys- C than SCr (90% vs 67%). Specificity for SCr was 97% whereas for Cys- C was 95%. Sensitivity for Cys-C was 80% while for SCr was 25%. SCr had PPV of 92% and NPV of 61% and for Cys- C it was 93% and 83% respectively. Asilioglu et al[20] also had higher accuracy and sensitivity of Cys- C (89% and 81% respectively) than SCr (66% and 24% respectively). A study by Murthy et al[19] demonstrated that patients suffering from AKI had significantly higher serum creatinine and in serum cystatin C level as compared to healthy subjects. It is well established factor that critically ill patients are more prone to have GFR alteration owing to hypoperfusion of kidneys secondary to shock or with the continuous uptake of drugs affecting kidneys.[21] However, it is very common to encounter serum creatinine level for few days until the stabilization phase reaches.

Our biggest drawback of the study was that it was a single centre, cross sectional study conducted at single point of time. The small sample size was another limitation. Other methods such as clearance of inulin, 125I-iothalamate clearance and 99mTc-DTPA was not discussed here.

CONCLUSION

Results demonstrated that Cys-C was better than SCr for the identification of renal impairment in critically ill patients. Hence, assessment of Cys-C is of great concern in AKI.

REFERENCES

1. Cockcroft DW, Gault MH. Prediction of creatinine clearance from serum creatinine. Nephron 1976;16:31-41.
2. National Kidney Foundation. K/DOQI clinical practice guidelines for chronic kidney disease: Evaluation, classification, and stratification. Am J Kidney Dis 2002;39:S1-266.
3. Froissart M, Rossert J, Jacquot C, Paillard M, Houillier P. Predictive performance of the modification of diet in renal disease and Cockcroft–Gault equations for estimating renal function. J Am Soc Nephrol 2005;16:763-73.
4. Kyhse-Andersen J, Schmidt C, Nordin G, Andersson B, Nilsson-Ehle P, Lindström V, et al. Serum cystatin C, determined by a rapid, automated particle-enhanced turbidimetric method, is a better marker than serum creatinine for glomerular filtration rate. Clin Chem 1994;40:1921-6.
5. Jung K, Jung M. Cystatin C: A promising marker of glomerular filtration rate to replace creatinine. Nephron 1995;70:370-1.
6. Kim KE, Onesti G, Ramirez O, Brest AN. Creatinine clearance in renal disease. A reappraisal. Br Med J 1969;4:11.
7. Randers E, Erlandsen EJ, Pedersen OL, Hasling C, Danielsen H. Serum cystatin C as an endogenous parameter of the renal function in patients with normal to moderately impaired kidney function. Clin Nephrol 2000;54:203-9.
8. Coll E, Botey A, Alvarez L, Poch E, Quintó L, Saurina A, et al. Serum cystatin C as a new marker for noninvasive estimation of glomerular filtration rate and as a marker for early renal impairment. Am J Kidney Dis 2000;36:29-34.
9. Randers E, Kristensen JH, Erlandsen EJ, Danielsen H. Serum cystatin C as a marker of the renal function. Scand J Clin Lab Invest 1998;58:585-92.
10. Knight EL, Verhave JC, Spiegelman D, Hillege HL, de Zeeuw D, Curhan GC, et al. Factors influencing serum cystatin C levels other than renal function and the impact on renal function measurement. Kidney Int 2004;65:1416-21.
11. Dharnidharka VR, Kwon C, Stevens G. Serum cystatin C is superior to serum creatinine as a marker of kidney function: A meta-analysis. Am J Kidney Dis 2002;40:221-6.
12. Newman DJ, Thakkar H, Edwards RG, Wilkie M, White T, Grubb AO, et al. Serum cystatin C measured by automated immunoassay: A more sensitive marker of changes in GFR than serum creatinine. Kidney Int 1995;47:312-8.
13. Ahlström A, Tallgren M, Peltonen S, Pettilä V. Evolution and predictive power of serum cystatin C in acute renal failure. Clin Nephrol 2004;62:344-50.
14. Hoek FJ, Kemperman FA, Krediet RT. A comparison between cystatin C, plasma creatinine and the Cockcroft and Gault formula for the estimation of glomerular filtration rate. Nephrol Dial Transplant 2003;18:2024-31.
15. Peralta CA, Shlipak MG, Judd S, Cushman M, McClellan W, Zakai NA, et al. Detection of chronic kidney disease with creatinine, cystatin C, and urine albumin-to-creatinine ratio and association with progression to end-stage renal disease and mortality. JAMA 2011;305:1545-52.
16. Rosner MH, Bolton WK. Renal function testing. Am J Kidney Dis 2006;47:174–83.
17. Stevens LA, Levey AS. Measurement of kidney function. Med Clin N Am 2005;89:457–73.
18. Che M, Wang X, Xie B, Huang R, Liu S, Yan Y, Zhu M, Lu R, Qian J, Zhang W, Gu L. Use of Both Serum Cystatin C and Creatinine as Diagnostic Criteria for Cardiac Surgery-Associated Acute Kidney Injury and Its Correlation with Long-Term Major Adverse Events. Kidney and Blood Pressure Research. 2019;44(3):415-25.
19. Murty MS, Sharma UK, Pandey VB, Kankare SB. Serum cystatin C as a marker of renal function in detection of early acute kidney injury. Indian journal of Nephrology. 2013 May;23(3):180.
20. Asilioglu N, Acıkgoz Y, Paksu MS, Gunaydin M, Ozkaya O. Is serum cystatin C a better marker than serum creatinine for monitoring renal function in pediatric intensive care unit?. Journal of tropical pediatrics. 2012 Dec 1;58(6):429-34.
21. Grubb A, Simonsen O, Sturfelt G, et al. Serum concentration of cystatin C, factor D and beta 2-microglobulin as a measure of glomerular filtration rate. Acta Med Scand 1985;218:499–503.