ISSN:0975-3583,0976-2833 VOL12,ISSUE04,2021

Usefulness of serum Cystatin C in comparison to serum creatinine as an early marker of acute renal disease- An Original Research

Dr. Vishal Bhargava[1],Dr.Krishana Gopal[2], Dr. Ram A Rawat[3], Dr.Richa Sijoria[4]

[1]Associate Professor, Department of Biochemistry GR Medical College Gwalior M.P;
[2]Associate Professor, Department of Biochemistry LLRM Medical College Meerut U.P;
[3]Associate Professor, Department of Cardiology GR Medical College Gwalior M.P;
[4]Department of Biotechnology SOS Jiwaji University Gwalior M.P

Corresponding author:
Dr RichaSijoria, Department of Biotechnology SOS Jiwaji University Gwalior M.P., India

ABSTRACT

Background: Acute kidney injury (AKI) is characterized by rapid decline in glomerular filtration rate (GFR). Cystatin C is 13-kDa cysteine protease inhibitor that is produced by all nucleated cells at a constant rate. Hence; the present study was conducted with the aim of assessing the usefulness of serum Cystatin C in comparison to serum creatinine as an early marker of acute renal disease.

Materials & methods:100 healthy subjects and 100 AKI patients were enrolled. Information such as age, gender, height, weight, comorbidities, personal history, drug history, presenting complaints and laboratory investigationswas obtained. The serum cystatin C and serum creatinine values were measured simultaneously and analysed. In the AKI study group, they were taken within 24 hours of onset of injury. All the results were recorded and analysed by SPSS software.

Results: Mean Serum Cystatin C levels among the patients of the AKI group and the control group was 2.35 mg/dL and 0.91 mg/dL respectively.Mean Serum creatinine levels among the patients of the AKI group and the control group was 1.97 mg/dL and 0.68 mg/dL respectively. Significant results were obtained while comparing the mean serum Cystatin C levels and Serum creatinine levels among the patients of the study group and the control group. Significant correlation of serum Cystatin C levels with AKI in comparison to serum creatinine levels.

Conclusion: In comparison to serum creatinine, Serum cystatin C is a better marker of renal function in AKI patients.

Key words: Cystatin C, Acute renal disease

INTRODUCTION

Acute kidney injury (AKI) is characterized by rapid decline in glomerular filtration rate (GFR). GFR is presently being monitored by serum creatinine concentration and calculated creatinine clearance using Cockcroft and Gault equation or Modification of Diet in Renal Disease study (MDRD) formula. However, serum creatinine does not increase until the GFR has moderately decreased (about 40 ml/min/1.73 m^2). This insensitivity for small to moderate decreases in GFR in creatinine blind GFR area (40-70 ml/min/1.73 m^2) gives a false sense of security and leads to late detection of kidney damage. All this makes serum creatinine less reliable for making therapeutic decisions in critically ill patients, such as decision to change nephrotoxic drugs or measures to increase renal perfusion.[1- 3]

However, the use of the serum creatinine level has many drawbacks, including variability according to age and sex and dependence on muscle mass, making it unsuitable for diagnosis of malnourished children. There is also a delay between the occurrence of significant renal damage and the increase in the serum creatinine level. Cystatin C is 13-kDa cysteine protease inhibitor that is produced by all nucleated cells at a constant rate. This compound is freely filtered by the glomeruli and completely catabolized by the proximal tubules with no secretion; thus, it is promising for use in glomerular filtration rate (GFR) estimation.[4- 6]Hence; the present study was conducted with the aim of assessing the usefulness of serum Cystatin C in comparison to serum creatinine as an early marker of acute renal disease.

MATERIALS & METHODS

Hence; the present study was conducted with the aim of assessing the usefulness of serum Cystatin C in comparison to serum creatinine as an early marker of acute renal disease. A total of 100 healthy subjects and 100 AKI patients were enrolled. Information such as age, gender, height, weight, comorbidities, personal history, drug history, presenting complaints and laboratory investigationswas obtained. The serum cystatin C and serum creatinine values were measured simultaneously and analysed. In the AKI study group, they were

ISSN:0975-3583,0976-2833 VOL12,ISSUE04,2021

taken within 24 hours of onset of injury. All the results were recorded and analysed by SPSS software. Student t test, chi-square test and Univariate regression curve was used for evaluation of level of significance.

RESULTS

Mean age of the subjects of the AKI group and the control group was 52.9 years and 49.2 years respectively. 78 percent of the subjects of the AKI group and 72 percent of the subjects of the control group were males.

Mean Serum Cystatin C levels among the patients of the AKI group and the control group was 2.35 mg/dL and 0.91 mg/dL respectively.Mean Serum creatinine levels among the patients of the AKI group and the control group was 1.97 mg/dL and 0.68 mg/dL respectively. Significant results were obtained while comparing the mean serum Cystatin C levels and Serum creatinine levels among the patients of the study group and the control group. Significant correlation of serum Cystatin C levels with AKI in comparison to serum creatinine levels.

Table 1: Comparison of demographic data

Variable	AKI patients	Controls
Mean age (years)	52.9	49.2
Males (%)	78	72
Females (%)	22	28

Table 2: Comparison of serum creatinine levels and serum Cystatin C levels

Variable	AKI patients	Controls	p- value
Serum Cystatin C (mg/dL)	2.35	0.91	0.00 (Significant)
Serum creatinine (mg/dL)	1.97	0.68	0.00 (Significant)

Table 3: Correlation of serum creatinine levels and serum Cystatin C levels in AKI

Variable	AKI patients				p- value
	Normal		Abnormal		
	n	%	n	%	
Serum Cystatin C	43	43	57	57	0.00 (Significant)
Serum creatinine	0	0	100	100	

DISCUSSION

The incidence of acute kidney injury (AKI) is increasing globally, affecting about 6% of all hospitalized patients in whom it is an independent predictor of mortality and morbidity. Much is now known about the epidemiology of AKI in the hospital-acquired and critical care settings. AKI occurring in a community setting is also common but quite distinct, and published data are scarce. Community-acquired renal dysfunction encountered in the emergency department (ED) is frequently caused by volume depletion, whereas hospital-acquired AKI often accompanies other organ disease processes and complicates their management and outcomes. In the ED, the clinician's priorities are to detect AKI early so that preventive and therapeutic approaches may be implemented in a timely manner, and to differentiate between prerenalazotemia (preR), chronic kidney disease (CKD), and intrinsic AKI. Unfortunately, neither is possible with serum creatinine (SCr) measurements, since changes in SCr lag behind both renal injury and renal recovery, and are influenced by several non-renal factors.[7- 9]Hence; the present study was conducted with the aim of assessing the usefulness of serum Cystatin C in comparison to serum creatinine as an early marker of acute renal disease.

In the present study, mean age of the subjects of the AKI group and the control group was 52.9 years and 49.2 years respectively. 78 percent of the subjects of the AKI group and 72 percent of the subjects of the control group were males.Mean Serum Cystatin C levels among the patients of the AKI group and the control group was 2.35 mg/dL and 0.91 mg/dL respectively.Mean Serum creatinine levels among the patients of the AKI group and the control group was 1.97 mg/dL and 0.68 mg/dL respectively. Leelahavanichkul A et al determined the renal contribution to sCysC handling with BiNx. sCysC and SCr were lower post-BiNx/CLP than post-BiNx alone, despite increased inflammatory and nonrenal organ damage biomarkers. Sepsis decreased CysC production in nephrectomized mice without changing body weight or CysC space. Sepsis decreased sCysC production and increased nonrenal clearance, similar to effects of sepsis on SCr.sCysC, SCr, and BUN were measured 6 h postsepsis to link AKI with mortality. Mice with above-median sCysC, BUN, or SCr values 6 h postsepsis died earlier than mice with below-median values, corresponding to a substantial AKI association with sepsis mortality in this model. sCysC performs similarly to SCr in classifying mice at risk for early mortality. They conclude that sCysC detects AKI early and better reflects iGFR in CLP-induced sepsis.[10]

In the present study, significant results were obtained while comparing the mean serum Cystatin C levels and Serum creatinine levels among the patients of the study group and the control group. Significant correlation of serum Cystatin C levels with AKI in comparison to serum creatinine levels. Safdar OY et al enrolled a total of

ISSN:0975-3583,0976-2833 VOL12,ISSUE04,2021

62 patients, and 32 were diagnosed with AKI according to the modified pRIFLE criteria (51.4 %). The area under the ROC curve for serum cystatin indicated that it was a good marker for the diagnosis of AKI at 0, 6, 12 and 24 h, with sensitivities of 78, 94, 94 and 83 %, respectively. However, the specificities of serum cystatin C at 0, 6, 12, and 24 h were 57, 57, 60 and 50 %, respectively. The optimal cutoff value was 0.645 mg/L. The area under the ROC for serum creatinine showed sensitivities of 50, 65.4, 69.2 and 57.7 % and specificities of 67.7, 70, 60 and 70 % at 0, 6, 12 and 24 h, respectively. The optimal cutoff value for serum creatinine was 30 μmol/l. Comparisons of ROC curves revealed that serum cystatin C was superior to serum creatinine for the diagnosis of AKI at 12 h ($p = 0.03$), but no differences were detected at 0, 6 or 24 h. Serum cystatin is a sensitive, but not a specific, marker for the diagnosis of AKI in critically ill children.[11]

CONCLUSION

In comparison to serum creatinine, Serum cystatin C is a better marker of renal function in AKI patients.

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 SocNephrol. 2005;16:763–73.
4. 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.
5. 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.
6. Ahlström A, Tallgren M, Peltonen S, Pettilä V. Evolution and predictive power of serum cystatin C in acute renal failure. ClinNephrol. 2004;62:344–50.
7. Mehta RL, Chertow GM. Acute renal failure definitions and classification: Time for change? J Am SocNephrol 14: 2178–2187, 2003
8. Hanley JA, McNeil BJ. The meaning and use of the area under a receiver operating characteristic (ROC) curve. Radiology 143: 29–36, 1982
9. Seronie-Vivien S, Delanaye P, Pieroni L, Mariat C, Froissart M, Cristol J-P. SFBC “Biology of renal function and renal failure” working group: Cystatin C: Current position and future prospects. ClinChem Lab Med 46: 1664–1686, 2008.
10. Leelahavanichkul A, Souza AC, Street JM, et al. Comparison of serum creatinine and serum cystatin C as biomarkers to detect sepsis-induced acute kidney injury and to predict mortality in CD-1 mice. Am J Physiol Renal Physiol. 2014;307(8):F939-F948
11. Safdar OY et al. Serum cystatin is a useful marker for the diagnosis of acute kidney injury in critically ill children: prospective cohort study. BMC Nephrology. 2016; 17: 130