ORIGINAL RESEARCH ARTICLE

Evaluation of Early Adjuvant Blood Marker in Acute Kidney Injury Diagnosis

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Abstract:

Background: - The acute kidney injury (AKI) is a common complication in the hospitalized patients. However its diagnosis at the earliest is challenging issue. Current diagnostic criteria for AKI poorly recognize early renal dysfunction causing delayed diagnosis.

Objective: Evaluation of the serum cystatin C along with routine kidney function tests such as urea, creatinine, sodium and potassium was done for earliest and effective marker for early diagnosis of AKI.

Method: In this retrospective study of 100 patients diagnosed on basis of clinical findings to have AKI, by the physician were estimated for serum cystatin C, creatinine, blood urea, serum sodium and potassium within 12 hrs. and results were compared with 100 normal healthy group.

Results: In this study 56% of patients of AKI had normal levels of serum creatinine within 12 hrs, while all patients (100%) had elevated serum cystatin C within 12 hrs. Hence, cystatin C in blood is an early marker for AKI than creatinine.

Conclusion: This study support the findings that cystatin C as an earliest marker and should be included in the KFT panel routinely done in hospital settings to diagnose AKI in early stage.

Keywords: AKI – Acute Kidney Injury, Cystatin C, Creatinine, Biomarker, Sodium, Potassium

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Introduction:

Acute kidney injury (AKI) occurs commonly worldwide upto 5-6% of the hospitalized patients [(1)] Despite progress in medical care, it is still associated with increased morbidly, mortality, length of hospital stay, costs, and post acute care resource utilization [(2),(3).] AKI is defined as a rapid (hours to days) decrease in renal excretory function with an accumulation of products of nitrogen metabolism, such as creatinine, urea and other clinically unmeasured waste products [(4).]

In routine clinical practice, creatinine is used to estimate renal function and accordingly, as a marker for diagnosing and staging of AKI [(4) & (5).]

A good biomarker is something that is easily measured and can be used as surrogate marker for diagnose or predict risk accurately (high specificity and sensitivity), promptly provide affordable but meaningful results, and should provide incrementally over existing markers or clinical characteristics. Medication, treatment and hospital stay also come at a cost, therefore simple and cheap tests have become increasingly necessary to decide how to target treatment [(6).]

This study was undertaken to evaluate the accuracy of cystatin- C as an early biomarkers of AKI as compared to routine markers such as creatinine, urea, sodium & potassium. Serum cystatin C is a low molecular weight protein produced by nucleated cells at a constant rate, is readily measurable using clinical laboratory platforms and does not increase with urinary tract infection, chronic non-renal disease and less effected by age and gender [(7,8)]

Material and Methods:

This study was carried out in Dept. of Medicine from June 2015 to December 17 at Government Medical College & Hospital, Aurangabad, Maharashtra. Clearance from

Ethical Committee of the institution was obtained.

Study group: 100 patients in the study group were selected based on age, sex, duration of symptoms with help of physician observing the patients.

Control group: For control group, 100 normal persons excluding hypertensive, cancers, HIV and with Tuberculosis were included in study.

Informed consent: Informed consent was taken from both subject and control group after explaining the purpose & procedure of study.

Collection of samples:

Collection of 5 ml venous blood samples in plain vacutainer were collected from both the groups on the day of admission within 12 hrs. under aseptic conditions. Blood was allowed to clot at room temperature for half an hour and then separated at 3000 rpm by using a remi-clinical centrifuge. Serum separated was used for the estimations.

Estimation of serum cystatin C was done by turbidometric immunoassay reagent kit on automatic clinical chemistry analyzer, serum creatinine by Jaffes kit method, serum sodium and potassium were measured by Flamephotometry using Bio-lab Diagnostic kits. The normal ranges for the above estimates are as follows:

Cystatin C	-	0.51-1.05 mg/dl
Creatinine	-	0.50-1.80 mg/dl
Urea	-	15-40 mg/dl
Sodium	-	135-145 mEq/Lit.
Potassium	-	3.5-4.5 mEq/Lit.

Results:

The characteristics of our study population are given in Table – I

Table –I

Characteristics	**AKI** (n=100)	**Normal** (n=100)
Age (yrs.)	53.8 ± 17.9	31.8 ± 14.8
Male %	81	90
Female %	19	10
Weight (kg)	64.7 ± 11.8	64.4 ± 12.6
Blood Urea (mg/dl)	60.5 ± 21.92	26.5 ± 9.19
Serum creatinine (mg/dl)	2.7 ± 1.13	0.75 ± 0.21
Serum Cystatin-C (mg/dl)	1.89 ± 0.29	0.45± 0.10
Serum Sodium	130 ± 2.82	137 ± 7.07
Serum Potassium	5.4 ± 0.84	3.55 ± 0.21

In Table II the variation of serum creatinine was significantly greater than that of serum cystatin C in both groups. The standard deviation of serum creatinine (0.21) is double that of serum creatinine C (0.10) in the healthy group, which indicates a wide fluctuation in serum creatinine compared to serum cystatin C in healthy population too. Although correlation between serum creatinine and serum cystatin C was highly significant in both groups, this implies that small changes in serum creatinine are best reflected by a proportionate rise in serum cystatin C in AKI, especially at lower values.

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Table –II

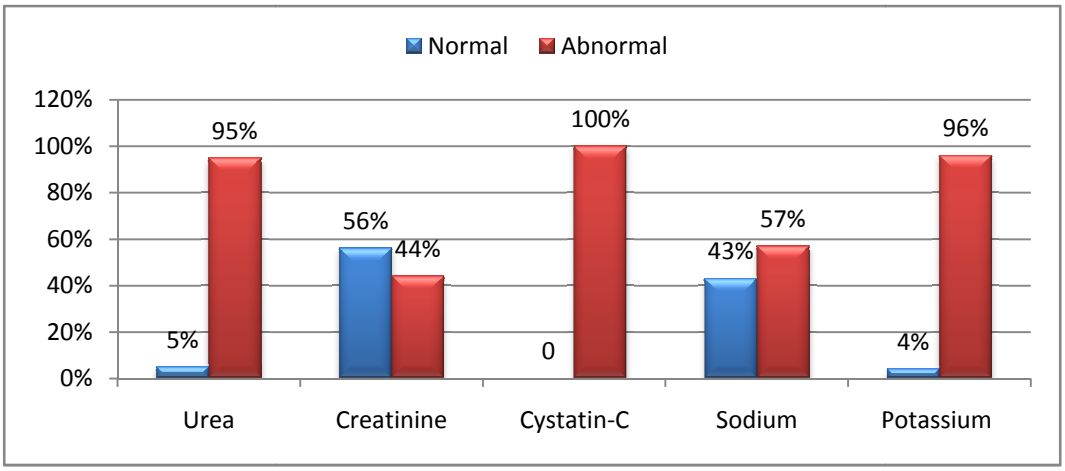
Parameter	AKI (n=100) (mean ± SD)	Normal (n=100) (mean ± SD)
Serum Creatinine	2.7± 1.13	0.75 ± 0.21
Serum Cystatic –C	1.89± 0.29	0.45 ± 0.10
P-value	<0.0001	<0.0001
correlation	Highly significant	Highly significant

In this study, it was found that in AKI group majority (56%) had normal creatinine values (0.9-1.8 mg/dl). This subset was in 'creatinine blind' range where serum creatinine values are normal with elevated cystatin C levels. All the 100 patients with AKI had deranged cystatic C levels (as in Table 3) and figure

Table –III

AKI	Normal	Abnormal
Urea	05%	95%
Creatinine	56%	44%
Cystatin-C	0	100%
Sodium	43%	57%
Potassium	04%	96%

Distribution of blood urea, serum creatinine, cystatin C, sodium and potassium in acute kidney injury as in figure below:



Discussion:

This study confirms the findings that serum cystatin- C start rising or elevated much before serum creatinine level start rising. In this way it helps for early detection of kidney injury within twelve hours and thereby helping in early therapeutic intervention. [9]

Since, single serum creatinine values do not provide any information about the AKI process, whether a patient is still in progression or recovery phase it may be necessary to use additional diagnostic tools or markers to diagnosis of AKI.

Significant progress has been made in detection and validation of new biomarkers of AKI to replace or complement serum creatinine. Creatinine negative, biomarkers-positive, patients appear to have a greater risk of complications, longer stay in hospital and higher mortality compared to patients without biomarker rise.[10]

Serum creatinine had higher standard deviation than serum cystatin- C in both subgroups AKI and healthy subgroups respectively. The variation of serum creatinine is significantly greater than serum cystatin C in both groups. Serum creatinine level increases with increase in muscle mass and protein intake. As blood levels of cystatin C are not significantly affected by age, gender or muscle mass, it is a better marker of AKI than serum creatinine. [11]

Also serum creatinine may take 24-36 hrs to rise after a definite renal insult. Also serum creatinine concentration is affected by drugs. There is also no standardized laboratory method for quantifying serum creatinine and substances like bilirubin or drugs may

interfere with certain analytical techniques, more commonly with Jaffe- based assays [12]. Creatinine, measured by labs for more than 100 years is used to estimate glomerular filtration rate. Creatinine helps determine magnitude of AKI, but it provides little information about underlying cause of kidney injuries and is less accurate for patients with low muscle mass and unusual diets. [13]

As in this study, the samples were collected within 12 hrs. of admission of patient and all tests were done, and found that 56% had normal creatinine but they had elevated cystatin- C and were in creatinine blind area. Moreover, all AKI patients had deranged cystatin- C. This confirms the findings that cystatin C is elevated much before serum creatinine levels start rising. Also cystatin- C does not have a blind area. Moreover, all AKI patients had deranged cystatin-C (100%). Serum cystatin-C has a higher sensitivity in identifying early kidney dysfunction, which is missed by relying on serum creatinine, urea, sodium or potassium, alone.

Cystatin -C represented promising sequential biomarker conditions in the blood AKI panel. An advantages of cystatin C is the commercial availability of standardized immunoephelometric assay kit which provides results in minutes, additionally, routine, clinical storage conditions, the presence of interfering substances and etiology of AKI do not affect serum cystatin- C measurement.[14]

As a markers of renal functions apart from creatinine, blood urea & serum electrolytes are done for routine analysis. 95% of this study group had increased blood urea level. Urea in blood not specific for determining kidney injury, but is a frequently determined for clinical indices for estimating renal function.

Electrolyte panel is frequently used to screen electrolyte or acid- base imbalance affecting bodily organ function. This study also had 96% cases of increased potassium level and slight decrease in sodium levels. Potassium used as most convincing electrolyte marker of renal failure. The combination of decreased filtration and secretion of potassium in distal tubule during renal failure cause increased plasma potassium. Hyperkalemia is the most significant and life-threatening complication of renal failure.[15,16]

In this study the decreased level of sodium observed and elevated serum potassium levels were found, as compared to control cases. In renal disease, the cause of decreased sodium and increased potassium is related with glomerular filtration rate and passive back diffusion through damaged tubular cells. This is due to malfunctioning of

aldosterone and renin-angiotensin system, impaired glomerular filtration and decreased reabsorption [17, 18].

Finally, since among the routine biomarker tests serum creatinine lag behind and does not provide a useful real time assessment of kidney damage. AKI is often diagnosed late in critically ill patients. Hence, cystatin C should be used routinely as a early diagnostic marker along with creatinine, urea, sodium and potassium in blood.

Conclusion:

From this study it can be concluded that serum cystatin-C is an excellent early diagnostic marker and hence should be included in the routinely done kidney function panel such as blood urea , serum creatinine, sodium and potassiumas an adjunctive and not alternative in the hospital settings to diagnose and to asses progression of acute kidney injury stages for proper line of treatment.

Conflict of interest: None to declare

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