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Association and prognostic value of serum Cystatin C, IL-18 and Uric acid in urological patients with acute kidney injury

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ABSTRACT

Purpose: To assess the role of serum Cystatin C, IL-18 and Uric acid in acute kidney injury (AKI) in urological patients, along with their prognostic significance.

Materials and methods: Prospective observational study included 61 cases, admitted in urology ward with baseline serum creatinine ≤1.5 mg/dL. All patients had at least one or more predisposing factors for AKI. Daily urine output and creatinine level were checked. Serum levels of biomarkers were measured at baseline and postoperatively after 24 h. Development of AKI and its outcome were analysed.

Results: Thirty nine patients (63.9%) developed AKI in the study. Patients with AKI were found to have a greater percentage rise of Cystatin C (118.7% v/s 81.8%, p = 0.005), IL-18 (59.0% v/s 25.5%, p = 0.004) and Uric acid (34.3% v/s 19.2%, p = 0.008) after 24 h. Absolute Uric acid level at day 1 was also significantly associated with AKI (5.18 ± 0.91 v/s 4.45 ± 0.86, p = 0.003). Risk stratification of AKI was poor for all biomarkers. Area under curve for Cystatin C, IL-18 and Uric acid was 0.715, 0.696 and 0.734 respectively. Renal function after 3 months, had a positive correlation with baseline creatinine and baseline Cystatin C levels (r = 0.56 & 0.39).

Conclusions: Postoperative serum Cystatin C, IL-18 and Uric acid after 24 h were significantly associated with AKI. Baseline Cystatin C had moderate capability to predict short term renal function.

1. Introduction

Acute kidney injury (AKI) is commonly defined as an abrupt decline in the renal function, clinically manifesting as a reversible acute increase in serum creatinine concentrations within 48 h. The diagnosis of AKI is usually based on either an increase of serum creatinine by ≥0.3 mg/dL and or the decrease in urine volume < 0.5 mL/kg/h for 6 h, as defined by KDIGO criteria. It is classified by Acute Kidney Injury Network (AKIN) staging system, which correlate well with severity and outcome [1]. Incidence of AKI varies globally and regionally. Western literature has described the AKI incidence of 21.6% in adults in hospitalized setting [2]. Recently a large cohort study has also reported the similar incidence rate of 19.6% globally [3]. Though a country wide study is not yet available in India, few studies have suggested an incidence rate between 16 and 17% [4,5].

Serum creatinine concentration is altered significantly by various non-renal factors such as body weight, race, gender, age, drugs, muscle metabolism, and oral protein intake [6]. Its role is questionable in early stages of AKI, as the patients are not in the steady state, hence serum creatinine may not rise upto 48–72 h after the initial insult [7].

The need for early detection of renal injury has lead to the identification of several biomarkers of AKI, that have been found elevated with clinical AKI. These biomarkers include both serum tests such as Cystatin C, LDH, Alkaline Phosphatase, IL-6, IL-18, Uric acid and urinary tests such as interleukin-18 (IL-18) and neutrophil gelatinase-associated lipocalin (NGAL) [8]. Various studies have examined the role of biomarkers in AKI, in patients of cardiac surgery, sepsis, cirrhosis and in ICU settings; however there is sparse data on urological patients. Uncertainty still exists, however, as to whether these biomarkers possess adequate prognostic accuracy for established AKI in urological patients.

Cystatin C, a non-glycosylated protein, is produced continuously by all nucleated cells and its concentration is only determined by GFR. Moreover, its concentration is not influenced much by age, gender, muscle mass, infections, and inflammatory or liver diseases. Several studies demonstrated the superiority of serum Cystatin C in comparison with creatinine in the detection of minor GFR reduction [9,10]. IL-18 is a inflammatory cytokines that has long been described as having both pro-and anti-inflammatory properties [11]. These have been found to correlate with onset and severity of AKI. Serum Uric acid (UA) is the potential marker, which is not only easy to measure and affordable, but also been found to predict the progression of AKI and renal replacement

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therapy (RRT) requirement particularly in patients underwent cardiac surgeries [12,13].

2. Materials and methods

2.1. Study design

Prospective observational study was conducted in the department of urology, from March 2015 to November 2016. Approval from the institutional ethical committee was obtained. Informed written consent was taken from all patients during enrolment.

2.2. Population characteristics

Patients with serum creatinine ≤1.5 mg/dL, along with minimum one predisposing factor for AKI were selected. All patients were from single origin and belonged to Indian population. Following predisposing factors were chosen: Renal surgery (PCNL, Nephrectomy, Ureterolithotripsy), renal trauma, age > 70 y, serum bilirubin > 2 mg/dL, chronic heart failure NYHA class III or IV or cardiac surgery, diabetes, hypertension, sepsis and surgery in emergency setting. Patients with serum creatinine > 1.5 mg/dL, hypothyroidism, hyperthyroidism, aortic aneurysm, treatment with corticosteroid, trimethoprim, cimetidine, diuretics and of age < 18 y were excluded from the study.

2.3. Study protocol

Patients underwent standard urological treatment according to the nature of their illness. Routine postoperative care was provided with special attention on daily urine output, serum creatinine measurement and eGFR calculation (Fig. 1). AKI was diagnosed by applying KDIGO guidelines as any of the following: 1) increase in serum creatinine by ≥0.3 mg/dL with 48 h, increase in serum creatinine to ≥1.5 times baseline or more within the last 7 days, or urine output < 0.5 mL/kg/h for 6 h. Patients were followed until resolution of AKI and final outcome in terms of recovered or not was recorded. Need for dialysis or any

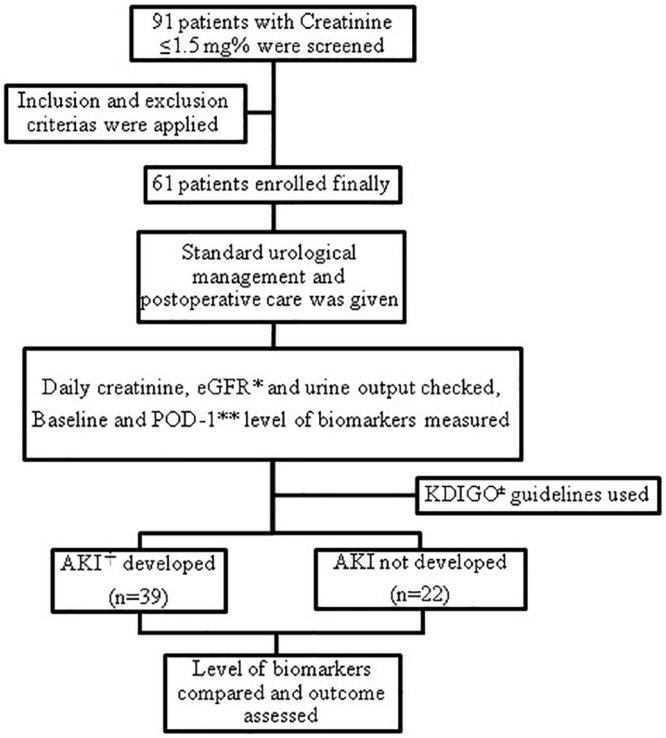

Fig. 1. Block chart showing study design and flow of study participants.

Table 1
Demographic parameters of study population.

Parameters	Mean	Median	Std. deviation	Minimum	Maximum
Age (y)	46.2	45.0	15.8	18	80
BMI (kg/m^2)	22.7	22.2	2.6	16.9	28.0
Baseline serum creatinine (mg/dL)	0.93	0.90	0.25	0.60	1.50
Baseline eGFR* (mL/min/1.73 m^2)	86.6	87.4	26.1	38.5	147.3

		Frequency	Percentage
AKI developed	Yes	39/61	63.9%
	No	22/61	36.1%
AKIN stages	1	34/39	87.2%
	2	4/39	10.2%
	3	1/39	2.6%

* eGFR- Estimated GFR by MDRD equation.

Table 2
Urological diagnosis of the patients in the study.

Diagnosis	n (%)	Management	n (%)
Renal stone	13 (21.3%)	Percutaneous nephrolithotomy	14 (22.9%)
Ureteric stone	10 (16.4%)	DJ stenting	3(4.9%)
Bladder stone	1 (1.6%)	OPEN Surgery	6 (9.8%)
Prostatomegaly with Hydronephrosis	7 (11.5%)	Percutaneous cystolithotripsy	1(1.6%)
Cancer prostate	1 (1.6%)	Radical nephrectomy (RN)	7 (11.5%)
Post PCNL Hematuria	1 (1.6%)	Partial Nephrectomy (PN)	1(1.6%)
Lower ureteric mass	2 (3.3%)	Prostatic Biopsy	1(1.6%)
Non-functioning kidney	5 (8.2%)	Radical cystectomy	5 (8.2%)
PUJ Obstruction	2 (3.3%)	DJ stent removal	1 (1.6%)
Renal mass	5 (8.2%)	Simple nephrectomy (SN)	5 (8.2%)
Ureteric mass	2 (3.3%)	TURP	5 (8.2%)
Ureteric stricture	1 (1.6%)	Bladder decompression	2 (3.3%)
Invasive bladder cancer	5 (8.2%)	UDS	1(1.6%)
Pelvic fracture	1 (1.6%)	Ureteroscopy	1(1.6%)
Post PCNL sepsis	1 (1.6%)	Ureteroscopic lithotripsy	8 (13.1%)
Prostatic abscess	1 (1.6%)		
Obstructing Megaureter	1 (1.6%)		
Renal hydatid cyst	1 (1.6%)		
Urethral injury	1 (1.6%)		
Total	61 (100.0%)	Total	61 (100.0%)

Table 3
Distribution of predisposing factors for AKI in the study participants.

Precipitating factors	Frequency (n)	Percent
Renal surgery	15	24.6
Diabetes (DM)	8	13.1
DM, hypertension (HTN)	3	4.9
Emergency admission (ER)	4	6.6
HTN	11	18.0
HTN, age > 70 years	3	4.9
HTN, Ischemic heart disease	1	1.6
Lt small kidney	1	1.6
Neurogenic bladder	1	1.6
Single kidney	1	1.6
Urosepsis (US)	10	16.3
US, ER	3	4.9
Total	61	100.0