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Urine biochemistry in septic and non-septic acute kidney injury: a prospective observational study☆,☆☆

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Abstract

Purpose: Determine whether there are unique patterns to the urine biochemistry profile in septic compared with non-septic acute kidney injury (AKI) and whether urinary biochemistry predicts worsening AKI, need for renal replacement therapy and mortality.

Materials and Methods: Prospective cohort study of critically ill patients with septic and non-septic AKI, defined by the RIFLE (Risk, Injury, Failure, Loss, End-Stage) criteria. Urine biochemistry parameters were compared between septic and non-septic AKI and were correlated with neutrophil gelatinase-associated lipocalin (NGAL), worsening AKI, renal replacement therapy (RRT), and mortality.

Results: Eighty-three patients were enrolled, 43 (51.8%) with sepsis. RIFLE class was not different between groups (P = .43). Urine sodium (UNa) < 20 mmol/L, fractional excretion of sodium (FeNa) < 1%, and fractional excretion of urea (FeU) < 35% were observed in 25.3%, 57.8%, and 33.7%, respectively. Septic AKI had lower UNa compared with non-septic AKI (P = .04). There were no differences in FeNa or FeU between groups. Urine NGAL was higher for FeNa≥1% compared to FeNa<1% (177.4 ng/mL [31.9-956.5] vs 48.0 ng/mL [21.1-232.4], P = .04). FeNa showed low correlation with urine NGAL (P = .05) and plasma NGAL (P = .14). There was poor correlation between FeU and urine NGAL (P = .70) or plasma NGAL (P = .41). UNa, FeNa, and FeU showed poor discrimination for worsening AKI, RRT and mortality.

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☆☆ Author contributions: SMB conceived the study, participated in its design and coordination, performed statistical analysis and drafted the manuscript. MB participated in the data collection and helped draft the manuscript. PD participated in the data collection and helped draft the manuscript. RB conceived the study, participated in its design, data interpretation, and helped to draft the manuscript. All authors read and approved the final manuscript.

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Conclusion: Urine biochemical profiles do not discriminate septic and non-septic AKI. UNa, FeNa, and FeU do not reliably predict biomarker release, worsening AKI, RRT or mortality. These data imply limited utility for these measures in clinical practice in critically ill patients with AKI.

1. Background

Acute kidney injury (AKI) is a common complication amongst critically ill patients and has an important modifying effect on mortality, kidney recovery, and resource utilization [1–3]. Sepsis is the most common predisposing factor for the development of AKI [2]. Septic AKI patients generally have a poorer prognosis when compared to AKI of non-septic origin [4–6]. Experimental data have suggested there may be important pathophysiologic differences between septic and conventional ischemic/toxic-induced AKI [7–9]. Considering these differences, discriminating septic and non-septic AKI may have clinical relevance and prognostic importance.

The diagnosis of AKI had traditionally relied on absolute or relative changes to conventional laboratory values (ie, serum creatinine) and urine output. These parameters, at selected thresholds, have been integrated into consensus definitions and classification schemes for AKI and were recently applied to the KDIGO Clinical Practice Guideline for AKI [10,11].

In addition, the diagnosis of AKI often integrates an assessment of urine biochemistry and derived indices (ie, urinary sodium [UNa], fractional excretion of sodium [FeNa], fractional secretion of urea [FeU]) as complementary data to further aid in the diagnostic evaluation and discrimination of the etiology of AKI. These urine biochemical tests have traditionally been used as a method to categorize AKI into states of "pre-renal azotemia", whereby AKI may be milder and reversible (UNa <20 mmol/L; FeNa $<1\%$; FeU $<35\%$), and "acute tubular necrosis" (ATN), whereby AKI is more severe and established (UNa >40 mmol/L; FeNa $>2\%$; FeU $>35\%$). In addition, no studies have utilized novel biomarkers of kidney "damage" such as neutrophil gelatinase-associated lipocalin (NGAL) to evaluate the diagnostic and prognostic value of urine biochemistry in AKI [12].

Few studies have evaluated and compared the diagnostic and prognostic value of urine biochemistry and derived indices in septic compared with non-septic AKI [13,14]. In fact, two systematic reviews have recently challenged the validity of routine urine biochemistry in septic AKI [15,16]. In addition, no studies have correlated novel biomarkers of kidney "damage", such as neutrophil gelatinase-associated lipocalin (NGAL), into an evaluation of the diagnostic and prognostic value of urine biochemistry in AKI.

We hypothesized there would be marked variation in the urine biochemical profile and derived indices among critically ill patients with septic compared with non-septic AKI that would preclude diagnostic and prognostic utility. Accordingly, our objectives were to describe: (1) the differences in the urine biochemical profile and derived indices between septic and non-septic AKI; (2) the association between urine biochemical profile and derived indices and the kidney damage biomarker neutrophil gelatinase-associated lipocalin (NGAL); (3) the association between urine biochemical profile and derived indices and worsening AKI; (4) the association between urine biochemical profile and derived indices and need for renal replacement therapy (RRT) and hospital mortality.

2. Methods

2.1. Study design

This was a prospective observational cohort study. The reporting of this study follows the STROBE (Strengthening the Reporting of Observational Studies in Epidemiology)

Table 1 Summary of baseline characteristics

Characteristic	Septic (n = 43)	Non-septic (n = 40)	*P*
Age (y) (mean [SD])	67.9 (16.3)	60.6 (16.3)	.04
Male sex (n, %)	23 (53.5)	27 (67.5)	.26
Weight (kg) [mean (SD)]	71.2 (15.4)	81.1 (17.8)	.01
Charlson Comorbidity Score (mean [SD])	4.1 (3.0)	2.4 (2.2)	.005
Cardiac disease (%)	41.9	55	.28
COPD (%)	27.9	12.5	.11
Diabetes mellitus (%)	20.9	25.0	.80
Liver Disease (%)	11.6	17.5	.54
Surgical admission (n, %)	22 (51.2)	26 (65.0)	.27
Cardiac surgery (n, %)	2 (9.1)	18 (69.2)	<.001
Emergency surgery (n, %)	19 (86.4)	4 (15.4)	<.001
APACHE II Score (mean [SD])	23.5 (5.4)	19.2 (8.9)	.008
SOFA Score (mean [SD])	8.2 (3.1)	6.3 (3.4)	.008
Mechanical ventilation (n, %)	26 (60.5)	33 (82.5)	.03
Vasoactive therapy (n, %)	34 (79.1)	25 (62.5)	.15
Shock (n, %)	38 (88.4)	30 (75.0)	.16