# Urinary Biomarkers of Acute Kidney Injury in Egyptian Patients With Liver Cirrhosis

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## OBJECTIVES

Acute kidney injury (AKI) in patients with cirrhosis is common. Up to 20 % of hospitalized patients with cirrhosis develop AKI and once AKI occurs there is a reported fourfold increased risk of mortality.

Typically, patients with decompensated liver cirrhosis have significant circulatory dysfunction which is characterized by a vasodilatory state, lower total peripheral resistance, activated renin-angiotensin-aldosterone system (RAAS) and finally renal arterial vasoconstriction.

The study was to assess the ability of urinary NGAL and IL-18 as early biomarkers of AKI and could discriminate types of AKI in patients with cirrhosis.

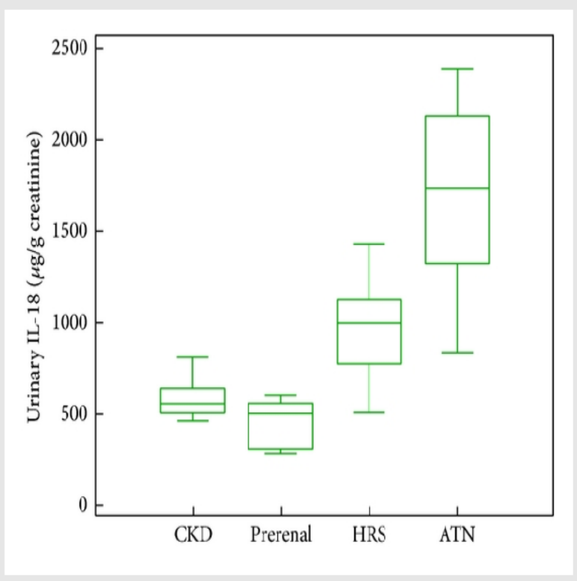
## METHODS

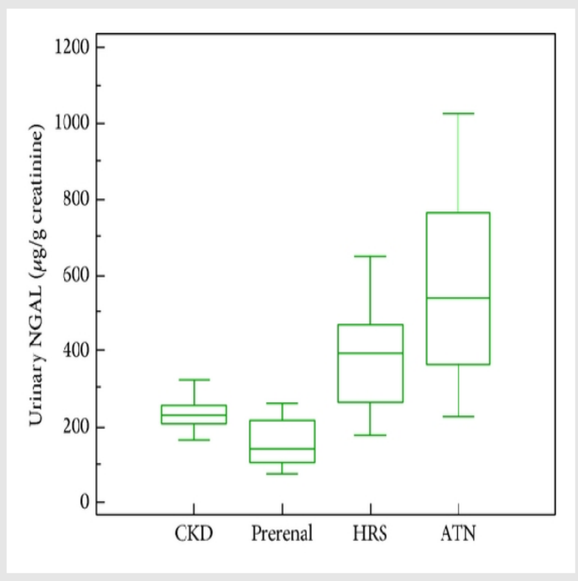
A cross-sectional study including 160 patients with cirrhosis admitted to the Liver Units at Zagazig University Hospitals from July 2012 to December 2012. Patients were classified into three groups: (I) nonascitic patients (n=42), (II) ascitic patients without renal impairment (n=50), and (III) ascitic patients with renal impairment (n=68). This classification was used because it reflects the different stages of cirrhosis. Patients with renal impairment were further divided into four subgroups: [A] prerenal azotemia, [B] chronic kidney disease (CKD) , [C] HRS , and [D] ATN. Urine samples for NGAL , IL-18 levels and routine biochemical investigation were done for all patients

Table 2: Characteristics of renal impairment patients.

| | CKD ($n$ = 15) | Prerenal ($n$ = 17) | HRS ($n$ = 14) | ATN ($n$ = 22) | $P$ |
|---|---|---|---|---|---|
| Serum creatinine (mg/dL) | 2.79 ± 0.8 | 1.76 ± 0.2 | 2.21 ± 0.79 | 2.7 ± 1.23 | 0.003 |
| Sodium (mEq/L) | 132 ± 6.71 | 132 ± 4.93 | 129 ± 5 | 133 ± 7.77 | 0.257 |
| Potassium (mEq/L) | 4.94 ± 0.8 | 4.39 ± 0.61 | 4.41 ± 0.955 | 4 ± 0.54 | 0.004 |
| Glomerular filtration rate (mL/min/1.73 $m^2$) | 35.6 ± 20.5 | 53.2 ± 13.84 | 44.3 ± 22.8 | 45.98 ± 47.48 | 0.475 |
| Mean arterial pressure (mmHg) | 89.5 ± 11.49 | 77.2 ± 14.2 | 74.86 ± 9.17 | 69.78 ± 15.35 | 0.0001 |
| Urine sodium (mEq/L) | 29.2 ± 7.81 | 29.3 ± 13.18 | 12.4 ± 5.6 | 62.68 ± 8.17 | 0.0001 |
| Urinary IL-18 ($\mu$g/g creatinine) | 582.34 ± 98.24 | 451.47 ± 121.73 | 953.5 ± 273 | 1687.1 ± 447 | 0.0001 |
| Urinary NGAL ($\mu$g/g creatinine) | 232.63 ± 41.31 | 161.15 ± 60.75 | 380.6 ± 132.32 | 580.51 ± 238.75 | 0.0001 |
| Fractional excretion of sodium (FeNa) (%) | 0.32 ± 0.17 | 0.54 ± 0.24 | 0.15 ± 0.07 | 4.05 ± 1.05 | 0.0001 |

CKD: chronic kidney disease, HRS: hepatorenal syndrome, and ATN: acute tubular necrosis.
Significant at $P < 0.05$; $P < 0.01$; and $P < 0.001$.




## RESULTS

Urinary NGAL was positively correlated with serum creatinine (p<0.001) , urinary IL-18 (p<0.001) ,Fractional excretion of Na(FeNa) (p<0.001) and mean blood pressure (p =0.005) in patients subgroups with renal impairment.

The cut- off value of urinary NGAL that differentiate between patients with AKI and those with other causes of renal impairment was 286.3 µg/g creatinine (AUROC curve is 0.909) with (sensitivity 95.5 %, specificity 76.1 %).

While urinary IL-18 was positively correlated to serum creatinine (p<0.001) ,FeNa (p<0.001) and mean blood pressure (p = 0.006) in patients subgroups with renal impairment.

The cut-off value of urinary IL-18 that differentiate between patients with AKI and those with other causes of renal impairment was 1119.6 µg/g creatinine (AUROC curve is 0.975), with (sensitivity 95.5 %, specificity 91.3 %)

## CONCLUSIONS

Urinary NGAL and urinary IL-18 have the ability to differentiate between AKI types in patients with cirrhosis. This could improve risk stratification for patients admitted to the hospital with cirrhosis, perhaps leading to early ICU admission, transplant evaluation, prompt initiation of HRS therapy and early management of AKI.

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