

Clinical Significance of NGAL and KIM-1 in acute kidney injury in patients with scrub typhus

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Background

The aim of this study is to investigate the clinical significance of neutrophil gelatinase-associated lipocalin (NGAL) and kidney injury molecule-1 (KIM-1) for acute kidney injury (AKI) in patients with scrub typhus.

Patients and Methods

From 2014 to 2015, 145 patients were diagnosed with scrub typhus. Of these, we enrolled 138 patients who were followed up until renal recovery or for at least 3 months. We measured serum and urine NGAL and KIM-1 levels and evaluated prognostic factors affecting scrub typhus-associated AKI.

Results

Table 1. The clinical and laboratory findings of the 138 patients with scrub typhus

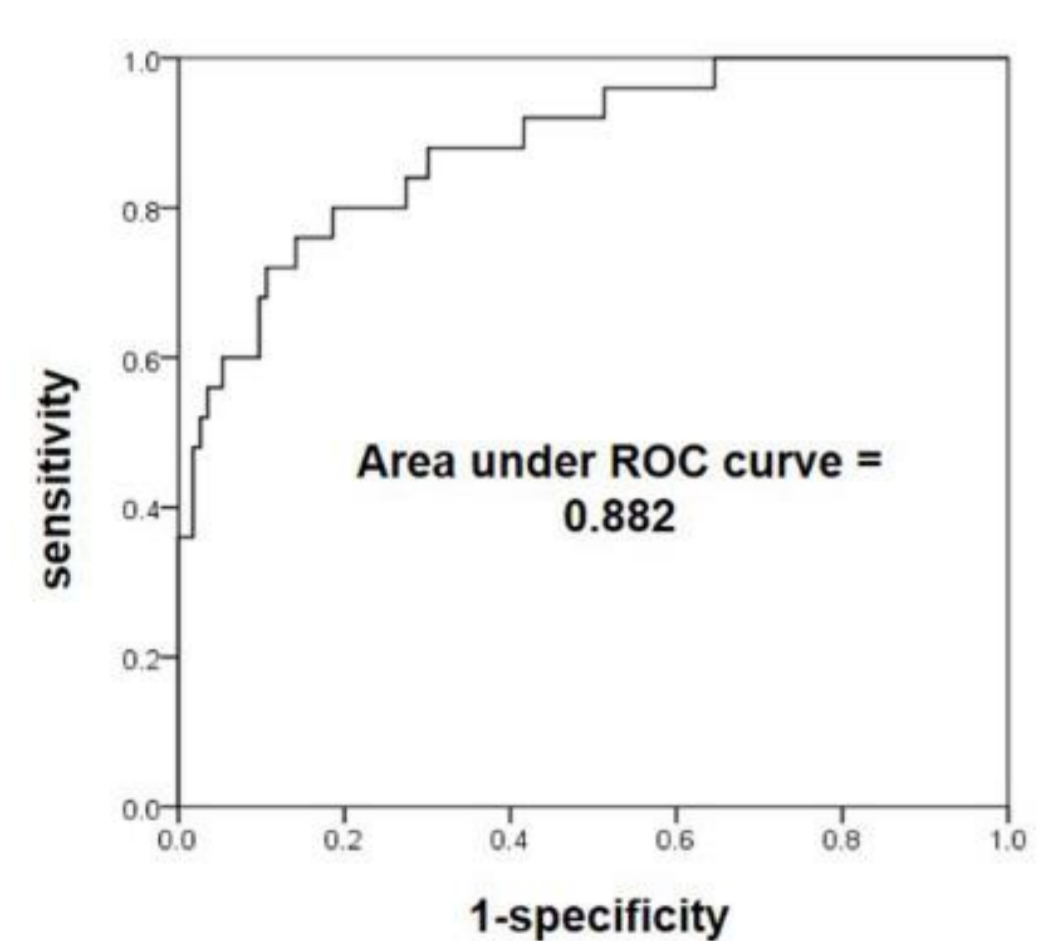
Characteristics	
Age, years	65 ± 13
Male, n (%)	49 (36)
Eschar, n (%)	130 (94)
Co-morbidity, n (%)	64 (46)
Diabetes, n (%)	26 (19)
Hypertension, n (%)	55 (40)
CKD, n (%)	9 (7)
Duration of hospital stay, days	6.4 ± 4.3
Fever, n (%)	132 (96)
Systolic BP (<90 mmHg), n (%)	8 (6)
ICU care, n (%)	5 (4)
Serum creatinine (mg/dl)	1.07 ± 0.58
eGFR _{adm} , ml/min/1.73m ²	64 ± 28
Serum ALT (IU/L)	82 ± 124
Total leukocyte count (× 10 ³ /mL)	7.73 ± 5.96
Platelet count (× 10 ³ /mL)	134 ± 55
Patient with baseline renal function, n (%)	73 (53)
Acute kidney injury, n (%)	25 (18)

Table 2. Comparison of baseline characteristics between non-AKI and AKI group

	AKI (n=25)	Non-AKI (n=113)	P-value
Age	74 ± 9	63 ± 12	< 0.01
Male, n(%)	12 (48)	37 (33)	NS
Duration of hospital stay, days	5.6 ± 2.5	10.2 ± 7.7	< 0.01
Comorbidity, n(%)	18 (72)	46 (41)	< 0.01
Diabetes, n (%)	10 (40)	16 (14)	< 0.01
Hypertension, n (%)	18 (72)	37 (33)	< 0.01
CKD, n (%)	8 (32)	1 (1)	< 0.01
Systolic BP (<90 mmHg), n (%)	5 (20)	3 (3)	< 0.01
Hemoglobin (mg/dl)	11.20 ± 1.80	13.12 ± 1.60	< 0.01
Leukocyte (× 10 ³ /mL)	11.00 ± 4.78	7.00 ± 5.97	< 0.01
Platelet count (× 10 ³ /mL)	123 ± 67	137 ± 52	NS
Total bilirubin level	0.81 ± 0.45	0.76 ± 0.36	NS
Serum albumin (mg/dl)	3.27 ± 0.50	3.78 ± 0.56	< 0.01
Serum ALT (IU/L)	56 ± 31	88 ± 136	NS
C-reactive protein (mg/dl)	9.28 ± 5.71	5.73 ± 4.04	< 0.01
Creatinine (mg/dl)	1.94 ± 0.91	0.87 ± 0.17	< 0.01
eGFR ml/min/1.73m ²	28 ± 13	72 ± 24	< 0.01
Serum NGAL (ng/mL)	404 ± 269	116 ± 78	< 0.01
Urine NGAL/Cr (ng/mg)	371 ± 672	27 ± 39	< 0.01
Serum KIM-1 (ng/mL)	0.80 ± 0.52	0.33 ± 0.68	< 0.01
Urine KIM-1/Cr (ng/mg)	4.04 ± 2.43	2.38 ± 1.89	< 0.01
IL-10 (pg/mL)	152 ± 163	62 ± 103	< 0.01
TNF-α (pg/mL)	55 ± 58	15 ± 15	< 0.01
IFN (pg/mL)	169 ± 297	156 ± 278	NS

Table 3. Clinical characteristics of 25 patients with AKI

		Risk (n=16)	Injury (n=6)	Failure (n=3)
NGAL	S-NGAL (ng/mL)	328 ± 270	530 ± 266	559 ± 125
	U-NGAL/Cr (ng/mg)	170 ± 392	280 ± 190	1629 ± 120
KIM-1	S-KIM-1 (ng/mL)	0.69 ± 0.57	0.88 ± 0.35	1.23 ± 0.37
	U-KIM-1/Cr (ng/mg)	3.36 ± 0.57	4.05 ± 0.35	7.68 ± 0.37
Cytokines	IL-10 (pg/mL)	86 ± 91	228 ± 174	338 ± 224
	TNF-α (pg/mL)	50 ± 58	44 ± 42	104 ± 82
	IFN (pg/mL)	154 ± 303	214 ± 362	162 ± 192
FENa < 1%, n (%)		15 (94)	3 (50)	1 (33)
Recovery of renal function within 72 h, n (%)		16 (100)	3 (50)	0



Serum NGAL cut off (ng/mL)	Sensitivity	Specificity
146.68	0.8	0.8
148.48	0.8	0.81
149.14	0.8	0.82
155.59	0.76	0.82

Figure. Receiver operating characteristic curve and performance characteristics for serum NGAL upon admission. The area under the ROC curve for the serum NGAL test is 88% (CI 0.808-0.956).

Table 4. Predictors of AKI (multivariate analysis)

Variables	Relative risk	95% CI		P value
		Lower	Upper	
Serum NGAL	1.04	1.003	1.019	0.006
Presence of CKD	67.01	2.120	2118.817	0.017

Summary and Conclusion

Serum NGAL might be an additive predictor for scrub typhus-associated AKI.