ASSOCIATION OF NEUTROPHIL GELATINASE-ASSOCIATED LIPOCALIN WITH INFLAMMATION, ORGAN DYSFUNCTION AND SURVIVAL IN SURGICAL SEPSIS

Authors: Bojic S¹, Kotur-Stevuljevic J², Memon L¹ Toskovic B¹, Simic-Ogrizovic S³

¹CHC Bezanijska Kosa, Belgrade, Serbia; ²Faculty of Pharmacy, Belgrade University, Serbia; ³Medical School, Belgrade University, Belgrade, Serbia

Background

- Systemic inflammation has a pivotal role in the pathogenesis of organ dysfunction in sepsis.
- Neutrophil gelatinase-associated lipocalin (NGAL), an established biomarker of acute kidney injury (AKI), is also an emerging biomarker of inflammation (1, 2, 3).

Goals

- To explore the association of NGAL with inflammation, organ dysfunction and survival in major abdominal surgical patients with sepsis.

Materials and Methods

- Prospective, observational study.
- 153 major abdominal surgical patients were divided into sepsis group (n = 53), operated controls (n = 50) and not-operated controls (n = 50). Patients were matched by age, gender, comorbidities and type of surgery.
- Blood and urine samples from the septic patients were collected daily during 96 h following admission to ICU and once from the controls.
- Serum (s-) and urine (u-) NGAL were measured using enzyme-linked immunosorbent assays (ABBOTT Diagnostics, IL, USA).
- White blood cell (WBC) count, C-reactive protein (CRP), procalcitonin (PCT), lactate, total bilirubin, platelet count and international normalized ratio (INR) were also measured.
- Occurrence of AKI, use of renal replacement therapy (RRT), vasopressors/inotropes, mechanical ventilation and 28-day survival were noted.
- American Society of Anesthesiology (ASA) physical status, Sequential Organ Failure Assessment (SOFA) and Acute Physiology and Chronic Health Evaluation II (APACHE II) score were calculated.

Results

Table 1. Baseline demographic and clinical characteristics of the patients with sepsis and both control groups

	Not-operated controls (N = 50)	Operated controls (N = 50)	Sepsis (N = 53)
Age (years)	60.00 [54.75 - 72.00]	65.00 [57.75 - 74.00]	70.00 [60.00 - 75.50]
Gender (male / female)	23 / 27	22 / 28	28 / 25
ASA (1 / 2 / 3 / 4 / 5)	0 / 50 / 0 / 0 / 0	0 / 50 / 0 / 0 / 0	2 / 47 / 4 / 0 / 0
Upper gastrointestinal / Colorectal Surgery	N.A.	9 / 41	18 / 35

Data are presented as frequencies or median and 25th - 75th percentile values. Mann-Whitney U.

- Patient groups were similar in age, gender, comorbidities (estimated as ASA physical status score) and type of surgery.
- On admission to ICU, patients with sepsis had significantly higher WBC count, CRP, PCT, lactate, bilirubin and INR levels, but lower platelet count compared to both control groups.

Figure 1. Dynamics of (A) serum NGAL and (B) urine NGAL in patients with sepsis in comparison to control groups

Data are expressed as minimum, maximum, median, and interquartile range. * significant difference (p < 0.05) compared to not-operated controls, # significant difference (p < 0.05) compared to operated controls. Mann-Whitney U test.

Table 2. Correlation analysis

	S-NGAL	U-NGAL
WBC count	0.136 *	0.112
CRP	0.320 *	0.034
PCT	0.281	- 0.092
Lactate	0.378**	0.116
Total bilirubin	0.183*	0.018
Platelet count	- 0.005	- 0.082
INR	0.139	0.148
APACHE II	0.432 **	0.319 **
SOFA	0.374 **	0.246 **

Data are presented as Kendal Tau-b correlation coefficients. * p < 0.05; ** p < 0.01.

Table 3. The association of NGAL with AKI, RRT, use of vasopressors/inotropes and mechanical ventilation

		S-NGAL (ng/mL) Average 0 h - 96 h		U-NGAL (ng/mL) Average 0 h - 96 h	
AKI	yes (n = 37)	179.4 [107.1 – 197.7]	p = 0.008	165.7 [74.0 – 200.3]	p = 0.004
	no (n = 16)	104.3 [97.0 – 174.6]		76.7 [43.0 – 165.4]	
RRT	yes (n = 7)	184.9 [170.8 – 225.2]	p = 0.032	223.8 [83.9 – 298.9]	p = 0.042
	no (n = 46)	164.2 [101.5 – 186.7]		107.4 [45.0 – 193.5]	
Vasopressor /inotropes	yes (n = 23)	185.8 [113.0 – 206.4]	p = 0.001	186.3 [82.5 – 211.3]	p < 0.001
	no (n = 30)	129.4 [99.4 – 177.5]		86.8 [42.2 – 161.4]	
Mechanical ventilation	yes (n = 41)	170.0 [102.4 – 197.7]	p = 0.908	148.8 [47.5 – 198.0]	p = 0.968
	no (n = 12)	171.7 [126.7 – 179.9]		153.5 [67.7 – 205.3]	

Data are presented as frequencies, median with 25th - 75th percentile interval and p values. P values represent significance of difference in NGAL values over 96 h following admission to ICU (linear mixed models analysis).

- 25 septic patients survived for 28 days after ICU admission.

Figure 2. Kaplan-Meier estimates of 28-day survival

Patients are stratified in quartiles. 1st quartile, 2nd quartile, 3rd quartile, 4th quartile. Log rank: (A) P_{S-NGAL} = 0.007 and (B) P_{U-NGAL} < 0.001.

Conclusions

- Higher NGAL levels were associated with inflammation, AKI, RRT, use of vasopressors/inotropes, higher lactate and bilirubin levels as well as with poor survival in major abdominal surgical patients with sepsis.

References

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