ROLE OF CD64 ON MONOCYTES AND HLA-DR ON NEUTROPHILS IN THE DIAGNOSIS OF SEPSIS AND OUTCOME OF CRITICALLY ILL PATIENTS

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Objective: Differentiation of infectious from non-infectious causes of Systemic Inflammatory Response Syndrome (SIRS) remains a challenge for Intensive Care Unit (ICU) physicians due to non-specific nature of symptoms and signs. The role of CD64 and HLA-DR antigen expression on monocytes and neutrophils have been established in the diagnosis of neonatal sepsis, while little data exist for adult critically ill patients. The objective is to evaluate their role in predicting infection in ICU patients with SIRS as compared to severity scores (SAPS II and SOFA score) and other biologic markers (CRP, ESR) in the differentiation of infectious and non-infectious causes of SIRS in ICU patients.

Methods: This single centre prospective cohort study was performed in the ICU of the University Hospital of Patras, Greece, during a 6 month period. All ICU patients, which developed SIRS during their stay, were enrolled. Patients with proven microbial etiology were assigned to the infectious causes, while patients with negative and more probable other etiology were assigned to the non-infectious causes. Flow cytometry was used to detect the presence of CD64 and HLA-DR antigens on the surface of neutrophils and monocytes. All cytometry variables are in comparison to control cytometry with IgG1. Epidemiologic data were collected from the ICU computerized database and patients' chart reviews. Statistical analysis was performed with SPSS ver. 19.0, as appropriate.

Results: Thirty-five patients developed SIRS due to non-infectious cause, while 27 patients had a proven infection (Table I). The optimum cutoff values and the diagnostic evaluation of variables in predicting infection in ICU patients with SIRS is depicted in Table II. The multivariate analysis revealed that the number of catheters, ≥44 points of SAPS II, <75.0% monocytes expressing CD64 and >0.45% neutrophils expressing HLA-DR were all significantly associated with an infectious SIRS. The overall mortality was 29% (18 patients). The multivariate analysis revealed that SAPS II score >44 points and multiple organ dysfunction syndrome were independently associated with mortality.

Table I. Infectious (and the causative pathogen) and non-infectious causes of Systemic Inflammatory Response Syndrome.

Infectious causes (n=27)		Non-infectious causes (n=35)	
Bloodstream infection	14 (51.9%)	Post-operative	23 (65.7%)
Catheter related bloodstream infection	5 (18.5%)	Multiple trauma	6 (17.1%0
Pneumonia	3 (11.1%)	Brain hemorrhage	3 (8.6%)
Peritonitis	3 (11.1%)	Pancreatitis	2 (5.8%)
Urinary tract infection	1 (3.7%)	Atelectasis	1 (2.9%)
Meningitis	1 (3.7%)	Myocardial infraction	1 (2.9%)
Bacteria isolated			
KPC-producing *Klebsiella pneumoniae*			12 (44.4%)
Acinetobacter baumannii			5 (18.5%)
Staphylococcus epidermidis			3 (11.1%)
Pseudomonas aeruginosa			2 (7.5%)
Escherichia coli			1 (3.7%)
Streptococcus pneumoniae			1 (3.7%)
Vancomycin-resistant *Enterococcus faecium*			1 (3.7%)
Candida parapsilosis			1 (3.7%)
Polymicrobial			1 (3.7%)

Table II. Sensitivity, specificity, PPV and NPV of variables in predicting infection in Intensive Care Unit patients with Systemic Inflammatory Response Syndrome

Variables	Cutt-off value	Sensitivity	Specificity	PPV	NPV	Accuracy
Neutrophils expressing HLA-DR (%)	>0.45%	91.7%	86.8%	81.5%	94.3%	0.879
Monocytes expressing HLA-DR (%)	<14%	44.4%	91.4%	80.0%	68.1%	0.679
Neutrophils expressing CD64 (%)	>8%	85.2%	68.6%	43.6%	67.7%	0.769
Monocytes expressing CD64 (%)	<75%	86.4%	80.0%	70.4%	91.4%	0.809
SAPS II score	>44 points	55.6%	85.7%	75.0%	71.4%	0.706
SOFA score	>10 points	63.0%	71.4%	63.0%	71.4%	0.672
CRP	>12.9 mg/dL	78.6%	76.9%	66.7%	85.7%	0.762

Conclusion: The percentage of monocytes expressing CD64 and especially the percentage of neutrophils expressing HLA-DR showed high sensitivity, specificity and accuracy in the diagnosis of sepsis, higher than those of SAPS II, SOFA and CRP. Their efficacy is also proved by the multivariate analysis for the prediction of sepsis in patients with SIRS.