



Evaluation of red cell distribution width (RDW) as a septic marker in comparison with clinical scores and C-reactive protein

Thesis

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بِسْمِ اللَّهِ الرَّحْمَنِ الرَّحِيمِ

قالوا

سبحانك لا علم لنا
إلا ما علمتنا إنك أنت
العليم العظيم

صدق الله العظيم

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List of Abbreviations

| | |
|--------------------|---|
| ACCP | : American College of Chest Physicians |
| ALT | : Alanine aminotransferase |
| ANOVA | : Analysis of variance |
| APACHE | : Acute Physiology Age and Chronic Health Examination |
| ARDS | : Acute respiratory distress syndrome |
| AST | : Aspartate aminotransferase |
| ATPs | : Adenosine triphosphates |
| ATS | : American Thoracic Society |
| AUCs | : The Areas Under the Curve |
| CBC | : Complete blood count |
| CI | : Cardiac index |
| CNS | : Central nervous system |
| CO ₂ | : Carbon dioxide |
| CRP | : C-reactive protein |
| cvaCO ₂ | : Central venous-to-arterial carbon dioxide |
| DIC | : Disseminated intravascular |
| ESICM | : European Society of Intensive Care Medicine |
| FE | : Fisher Exact test |
| FIO ₂ | : Fraction of Inspired Oxygen |
| HMGB1 | : High-mobility group box 1 |
| I/R | : Ischemic/reperfusion |
| ICU | : Intensive care unit |

List of Abbreviations

| | |
|--------------------|---|
| IL | : Interleukin |
| IV | : Intravenous |
| LPS | : Lipopolysaccharides |
| MAP | : Mean arterial pressure |
| MC | : Monte Carlo test |
| MCV | : Mean corpuscular volume |
| MIF | : Migration inhibitory factor |
| MODS | : Multiple organ dysfunction syndrome |
| mvaCO ₂ | : Mixed venous-to-arterial carbon dioxide |
| NPV | : Negative predictive value |
| PAMP | : Pathogen associated molecular patterns |
| PCT | : Procalcitonin |
| PMNs | : Polymorphonuclear cells |
| PPV | : Positive predictive value |
| PRR | : Pattern recognition receptors |
| RBCs | : Red blood cells |
| RDW | : Red blood cell distribution width |
| ROC | : Receiver Operating Curve |
| RRT | : renal replacement therapy |
| rs | : Spearman coefficient |
| SaO ₂ | : Arterial oxygen saturation |
| SAPS | : Simplified Acute Physiology Score |
| SCCM | : Society of Critical Care Medicine |
| ScvO ₂ | : Central venous oxygen saturation |

List of Abbreviations

| | |
|------|---|
| SD | : Standard deviation |
| NK | : natural killer |
| SIRS | : Systemic inflammatory response syndrome |
| SIS | : Surgical Infection Society |
| SOFA | : Sequential Organ Failure Assessment |
| T | : Student t-test |
| TNF | : Tumor necrosis factor |
| TLR | : Toll – like receptors |
| UG | : Ungraded |
| X2 | : Chi Square test |

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Introduction

Severe sepsis is the most common cause of death for patients admitted to the critical care units (*Farag et al., 2013*).

Sepsis is a multifaceted host response to an infecting pathogen that may be significantly amplified by endogenous factors (*Wiersinga et al., 2014*). Sepsis is defined as life-threatening organ dysfunction caused by a dysregulated host response to infection. This emphasizes the primacy of the non-homeostatic host-response to infection, the potential lethality that is considerably in excess of a straightforward infection, and the need for urgent recognition (*Singer et al., 2016*).

Sepsis, the inflammatory response to infection, affects millions of patients worldwide. However, its effect on overall hospital mortality has not been measured (*Liu et al., 2013*).

Sepsis, a syndrome of physiologic, pathologic, and biochemical abnormalities induced by infection, is a major public health concern in USA. The reported incidence of sepsis is increasing (*Gaieski et al., 2013*), likely reflecting

aging populations with more co-morbidities, greater recognition (*Dellinger et al., 2013*). Although the true incidence is unknown, conservative estimates indicate that sepsis is a leading cause of mortality and critical illness worldwide (*Fleischmann et al., 2015*).

Severity of organ dysfunction has been assessed with various scoring systems that quantify abnormalities according to clinical findings, laboratory data, or therapeutic interventions. The predominant score in current use is the Sequential Organ Failure Assessment (SOFA) (*Kaukonen et al., 2015*).

Nonspecific Systemic inflammatory response syndrome (SIRS) criteria such as pyrexia or neutrophilia will continue to aid in the general diagnosis of infection. These findings complement features of specific infections (e.g.; rash, lung consolidation, dysuria, peritonitis) that focus attention toward the likely anatomical source and infecting organism. Sepsis involves organ dysfunction, indicating a pathobiology more complex than infection plus an accompanying inflammatory response alone (*Cecconi et al., 2014*).

Early recognition of sepsis is not always straightforward and clinical signs at presentation can be misleading and very heterogeneous due to frequent comorbidities. In the emergency setting therefore an urgent need for a reliable diagnostic procedure, allowing early discrimination between SIRS and sepsis, is mandatory. Biomarkers, such as C-reactive protein (CRP) and procalcitonin (PCT), introduced among the diagnostic criteria of sepsis (*Dellinger et al., 2013*), could contribute to promptly identify patients affected by sepsis, severe sepsis and septic shock who could benefit from quick and appropriate therapy. C-reactive protein is one of the commonest biomarkers that are used during the management of sepsis. It was seen by some researchers to be significantly higher in sepsis patients compared to non-infectious SIRS (*El-Shafie et al., 2017*).

C-reactive protein production is a part of a larger picture of the acute phase response. This is principally regulated by the cytokines IL-6, Tumor necrosis factor alpha (TNF- α), and IL-1 β are also regulatory mediators of CRP synthesis. C-reactive protein is directly involved in clearance of microorganisms. It causes activation of

neutrophils and enhances natural killer (NK) cell activity (*Farag et al., 2013*).

Inflammatory biomarkers commonly used in clinical practice (CRP) are influenced by nonspecific systemic inflammatory responses, which are mediated by the innate immune response. Therefore, it is recommended that multiple biomarkers should be evaluated simultaneously (multimarker strategy) and that plasma concentrations of these biomarkers should be determined repeatedly. Many potential biomarkers have been tested as diagnostic and prognostic tools for the management of antimicrobial therapy in septic patients (*Franeková et al., 2017*).

Aim of the Work

The aim of our study is to evaluate the level of RDW, CRP and clinical scores "SOFA and APACHI" as markers in patients with sepsis and their levels on the outcome and resolution of sepsis in ICU.