



Comparative study between red cell distribution width (RDW) and serum lactate as prognostic factors for severe sepsis and septic shock

Thesis

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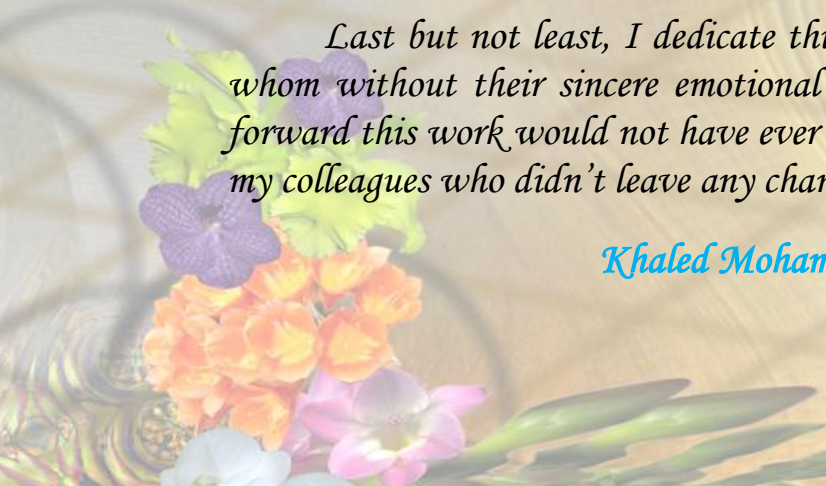
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List of Abbreviations

ABGs	: Arterial Blood Gases
APACHE	: Acute Physiology and Chronic Health Evaluation
ATPs	: Adenosine triphosphates
AVP	: Arginine vasopressin
CBC	: Complete blood count
CD14	: Cluster of differentiation 14
ChT	: Chitotriosidase
Cr	: Creatinine
ECG	: Electrocardiogram
GCS	: Glasscow coma score
HMGB1	: High-mobility group box 1
HR	: Heart Rate
I/R	: Ischemic/reperfusion.
IV	: Intravenous
LBP	: Lipopolysaccharide-binding protein
LPS	: Lipopolysaccharides
MAP	: Mean Arterial Pressure
MCV	: Mean corpuscular volume
MIF	: Migration inhibitory factor
PAMP	: Pathogen associated molecular patterns
PCT	: Procalcitonin
PMNs	: Polymorph nuclear cells
proADM	: Proadrenomedullin
PRR	: Pattern recognition receptors
Qsofa	: Quick Sepsis-Related Organ Failure Assessment
RBC	: Standard deviation in red blood cell
RDW	: Red cell distribution width
RR	: Respiratory Rate
SCCM	: Society of Critical Care Medicine

List of Abbreviations (Cont.)

sCD14	: Soluble cluster of differentiation 14
SD	: Standard deviation
SIRS	: Systemic inflammatory response syndrome
SOFA	: Sequential Organ Failure Assessment
SSC	: Surviving Sepsis Campaign
suPAR	: Soluble urokinase plasminogen activator receptor
TLC	: Total leucocytic count
TLR	: Toll-Like Receptors
TNF	: Tumor necrosis factor
uPAR	: Urokinase plasminogen activator receptor
VRE	: Vancomycin-resistant enterococci

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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 (*Angus and van der Poll, 2013; 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 (*Escobar et al., 2013; 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 (*Vincent et al., 2014; 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) (*Churpek et al., 2015; Kaukonen et al., 2015*).

Nonspecific 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 (*Farag et al., 2013; El-Shafie et al., 2017*).

The red cell distribution width (RDW) is a numerical measure of RBC variability and heterogeneity. RDW values are used to analyze the type of anemia (Shaikh and Rao, 2017). Recent studies have reported that RDW is associated with prognosis in critically ill patients, sepsis in elderly (*Mahmood et al., 2014; Shaikh and Rao, 2015*).

The erythrocyte distribution width (RDW) parameter quantifies the heterogeneity of RBC volume as the ratio of the standard deviation of RBC volume to the mean corpuscular volume. It is calculated as part of a routine automated complete blood count (CBC) and has been associated with a number of disease states including cardiovascular disease, cancer and diabetes (*Salvagno et al., 2015*). Retrospective and prospective studies of critically ill patients have reported that increased RDW is also a strong and independent risk factor of sepsis and septic shock mortality (*Kim et al., 2013; Sadaka et al., 2013; Bateman et al., 2017*).

Until recently, septic shock was considered to be composed of three components, including systemic arterial hypotension, tissue hypoperfusion associated with organ dysfunction, and hyperlactatemia (*Vincent and DeBaker, 2013*). According to the new definition of this issue (*Hari et al., 2016*), septic shock can be diagnosed under two conditions. The first condition is persistent hypotension after fluid resuscitation and requiring vasopressors to maintain

MAP >65 mmHg. The second condition is serum lactate level >2 mmol/L. Based on this pathophysiology; new definition of septic shock can be explained although serum lactate level of 2 mmol/L (18.2 mg/dL) is normal value. (*Lee and An, 2016*).

Septic shock status with liver dysfunction and acute kidney injury elevate lactate levels because of decreased lactate clearance. Lactate clearance at a discrete time point is an important prognostic factor compared to initial serum lactate level in severe sepsis (*Lee et al., 2015*).

Aim of the Work

The aim of our study is to evaluate the level of RDW and Lactate as markers in patients with sepsis and detect their levels on the outcome and resolution of septic shock in ICU.

Septic Shock

Background:

Over many years, the terms sepsis and septicemia have referred to several ill-defined clinical conditions present in a patient with bacteremia. Definitions have been started since 1914, when Schottmueller wrote, “Septicemia is a state of microbial invasion from a portal of entry into the blood stream which causes sign of illness.” In practice, these 2 terms have often been used interchangeably; however, only about half of patients with signs and symptoms of sepsis have positive results on blood culture (*Singer et al., 2016*).

Serious bacterial infections at any site in the body, with or without bacteremia, are usually associated with important changes in the function of every organ system in the body. These changes are mediated mostly by elements of the host immune system against infection. Alteration in organ function can vary widely, ranging from a mild degree of organ dysfunction to frank organ failure (*Ranieri et al., 2012*).

Definition of sepsis:

Sepsis is defined as life-threatening organ dysfunction due to dysregulated host response to infection, and organ dysfunction is defined as an acute change in total Sequential Organ Failure Assessment (SOFA) score greater than 2 points secondary to the infection cause (*Seymour et al., 2016*).