



# **Predictors of Morbidity and Mortality in Severe Sepsis and Septic Shock**

*Essay*

Submitted for partial fulfillment of The Master Degree in Intensive Care

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## العلامات المرضية ومؤشرات الوفاة في حالات تسمم الدم □ والصدمة التسممية

رسالة

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# *Dedication*

*My work is dedicated to:*

*My Great Good Allah,*

*&*

*My beloved Supervisors*

*Whose efforts and  
guidance made me  
able to serve this  
noble*

*profession of  
medical science.*

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## *List of Abbreviations*

<b>ALI</b>	: Acute Lung Injury
<b>ALT</b>	: Alanine Aminotransferase
<b>APACHE</b>	: Acute Physiology and Chronic Health Evaluation
<b>aPTT</b>	: Activated Partial Thromboplastin Time
<b>ARDS</b>	: Acute Respiratory Distress Syndrome
<b>AST</b>	: Aspartate Aminotransferase
<b>ATS</b>	: American Thoracic Society
<b>COPD</b>	: Chronic Obstructive Pulmonary Disease
<b>CPAP</b>	: Continuous Positive Airway Pressure
<b>CPIS</b>	: Clinical Pulmonary Infection Score
<b>CRP</b>	: C-Reactive Protein
<b>CVP,</b>	: Central Venous Pressure
<b>CXR</b>	: Chest X-Ray
<b>DIC</b>	: Disseminated Intravascular Coagulation
<b>ED</b>	: Emergency Department
<b>EGDT</b>	: Early-Goal-Directed Therapy Bundle
<b>EHR</b>	: Electronic Health Record
<b>ESICM</b>	: European Society of Intensive Care Medicine
<b>FiO<sub>2</sub></b>	: Fraction of Inspired Oxygen
<b>GCS</b>	: Glasgow Coma Scale
<b>HMGB</b>	: High-Mobility Group Box
<b>HR</b>	: Heart Rate
<b>ICD-9</b>	: International Classification of Diseases, Ninth Revision
<b>ICU</b>	: Intensive Care Unit
<b>IL</b>	: Interleukin
<b>INR</b>	: International Normalized Ratio
<b>LOD</b>	: Logistic Organ Dysfunction
<b>MAP</b>	: Mean Arterial Pressure;
<b>MAP</b>	: Mean Arterial Pressure
<b>MAP.</b>	: Mean Arterial Pressure
<b>MEWS:</b>	: Modified Early Warning Score
<b>MODS</b>	: Multiple Organ Dysfunction Syndrome
<b>MOFS</b>	: Multiple Organ Failure Syndrome
<b>MPM</b>	: Mortality Prediction Model
<b>NP</b>	: Natriuretic Peptides
<b>ODIN</b>	: Organ Dysfunction and Infection
<b>PaCO<sub>2</sub></b>	: Arterial Carbon Dioxide Tension
<b>PaO<sub>2</sub></b>	: Partial Pressure of Oxygen.

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## *List of Abbreviations*

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<b>PCT</b>	: Procalcitonin
<b>PE</b>	: Pulmonary Embolism
<b>PEEP</b>	: Positive End-Expiratory Pressure
<b>PT</b>	: Prothrombin Time
<b>qSOFA</b>	: Quick SOFA
<b>RR</b>	: Respiratory Rate
<b>RT-PCR</b>	: Real-Time Polymerase Chain Reaction
<b>SAPS</b>	: Simplified Acute Physiology Score
<b>SBP</b>	: Systolic Blood Pressure
<b>SIRS</b>	: Systemic Inflammatory Response Syndrome
<b>SIS</b>	: Surgical Infection Society
<b>SOFA</b>	: Sequential Organ Failure Assessment
<b>TNF</b>	: Tumor Necrosis Factor
<b>TRIOS</b>	: Three-Day Recalibrating ICU Outcomes Score
<b>VAP</b>	: Ventilator-Associated Pneumonia
<b>VCAM-1</b>	: Vascular Cell Adhesion Molecule 1
<b>WBC</b>	: White Blood Cell

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## **Introduction**

In 1992, an international consensus panel defined sepsis as a systemic inflammatory response to infection, noting that sepsis could arise in response to multiple infectious causes and that septicemia was neither a necessary condition nor a helpful term (*Levy et al., 2003*). Instead, the panel proposed the term “severe sepsis” to describe instances in which sepsis is complicated by acute organ dysfunction, and they defined “septic shock” as sepsis complicated by either hypotension that is refractory to fluid resuscitation or by hyperlactatemia (*Angus and van der Poll., 2013*).

New Sepsis definition announced by the 45th annual critical care congress in February 2016 as suspected or documented infection plus one of sequential organ failure assessment (SOFA) score or SOFA score plus hypotension (systolic Bp  $\leq 100$  mmhg) or altered conscious level (GCS  $\leq 13$ ) or tachypnea ( $\geq 22$  respirations/min) (*Singer et al., 2016*).

Admission acute physiology, age, chronic health evaluation (APACHE) II score is a standard predictor of mortality in critically-ill patients, including septic patients. It is applicable in the majority of critically-ill patients and extensively validated in several countries due to its simplicity as a predictor of mortality. The score is obtained from the patient’s age and the worst values of (12)

physiological parameters within the first (24) hours such as body temperature, mean arterial blood pressure, pulse, arterial pO<sub>2</sub>, serum creatinine, potassium, sodium, hematocrit, white blood cell count, glasgow coma scale and respiratory rate. The higher the APACHE II score, the higher the mortality rate. Other scores like SOFA which correlate closely with mortality (the highest SOFA score 48 hours post admission than on admission suggest high mortality), multiple organ dysfunction (MODS) and clinical pulmonary infection (CPIS) scores (*Hermans et al., 2012*).

A variety of other predictors of mortality in patients with sepsis was evaluated in clinical studies, including inflammatory markers such as C-reactive protein (CRP), lactate clearance, procalcitonin, cardiac biomarkers such as troponin and ejection fraction (EF) and individual organ system failures (*Vorwerk et al., 2009*).

We can't forget the role of radiological studies like Echocardiography, ultrasound, computed tomography and magnetic resonance imaging. The majority of patients in the mortality group had older age, higher lactate, lower albumin, and higher international normalized ratio, ED intubation, and intensive care unit admission (*Lagu et al., 2012*).

Severe sepsis and septic shock are time- dependent disease processes. Multiple organ dysfunction management

overlaps many of the principles used to approach severe sepsis and septic shock. These includes early source control, early resuscitation and appropriate organ support. Initial severe sepsis treatment can be divided into care bundles. The surviving sepsis campaign endorses a 3 – hour and 6-hour bundles. These bundles are then augmented with recommended supportive care measures (*Dellinger et al., 2012*).

## **Aim of the study**

To illustrate how to diagnose sepsis and determine markers of morbidity and mortality in patients with sepsis and septic shock.

## **Definitions of Sepsis and Causes**

### **Historical Overview of Sepsis and Septic Shock:**

Over the past years, the terms sepsis and septicemia have been referred to several ill-defined clinical conditions present in a patient with bacteremia. Septicemia is defined as a state of microbial invasion from a portal of entry into the blood stream which causes signs of illness. In practice, about half of patients with signs and symptoms of sepsis have positive results on blood culture, yet, not all patients with bacteremia have manifestations of sepsis (*Kumar et al., 2006*).

In the past few decades, the discovery of endogenous mediators of the host response has led to the recognition that the clinical syndrome of sepsis is the result of excessive activation of host defense mechanisms rather than the direct effect of microorganisms. Sepsis and its co-morbidities represent a series of clinical and pathophysiologic severity. Serious bacterial infections at any site in the body, with or without bacteremia, are usually accompanied with important changes in the function of every organ or system in the body. These changes are mediated mostly by elements of the host immune system against infection (*Surbatovic et al., 2013*).

Although hyperlactetemia is commonly seen in severe sepsis, its relationship to hypoperfusion is questionable and is more often due to the acute inflammatory state, impaired lactate clearance, and nonoxidative phosphorylation lactate production Shock is present when volume replacement fails to increase blood pressure to acceptable levels and when associated clinical evidence indicates inadequate perfusion of major organ systems, with progressive failure of organ system functions (*Surbatovic et al., 2013*).

The basis of sepsis is occurrence of infection accompanied with a systemic inflammatory response resulting in physiologic changes at the capillary endothelial level. Diagnosis becomes difficult when a localized infection become systemic and requires more hemodynamic support. No criterion standard exists for the diagnosis of endothelial dysfunction, and patients with sepsis may not initially present with frank hypotension and overt shock (*Singer et al., 2016*).

### **Definitions:**

Bacteremia is the presence of viable bacteria in the blood and is found only in about 50% of cases of severe sepsis and septic shock, whereas 20% to 30% of patients will have no microbial cause identified from any source (*Nguyen et al., 2006*).