# PROCALCITONIN IN REDUCING THE DURATION OF ANTIBIOTIC THERAPY IN SEPTIC CRITICALLY ILL PATIENTS

Thesis

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in Anaesthesiology

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وأنزل الله عليك
الكتاب والحكمة
وعَلَّمَكَ مَا لَمْ تَكُن تَعْلَمُ
وكَانَ فَضْلُ اللَّهِ عَلَيْكَ
عَظِيماً
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*First and above all thanks to **ALLAH**.*

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✍ Amr Mohamed El-Sayed Ahmed Shaaban

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## List of Abbreviations

| | |
|---|---|
| **ALI** | **Acute lung injury** |
| **ARDS** | **Acute respiratory distress syndrome** |
| **BBB** | **Blood-brain barrier** |
| **CDAD** | **Clostridium difficile-associated diarrhea** |
| **CRP** | **C-reactive protein** |
| **DIC** | **Disseminated intravascular coagulation** |
| **ED** | **Emergency department** |
| **ESBL** | **Extended-spectrum beta lactamases** |
| **FUO** | **Fever of unknown origin** |
| **HPV** | **Hypoxic pulmonary vasoconstriction** |
| **ICU** | **Intensive care unit** |
| **IL** | **interleukins** |
| **MDR** | **Multi-drug resistant** |
| **MODS** | **Multiple organ dysfunction syndrome** |
| **PCT** | **Procalcitonin** |
| **RTIs** | **Respiratory tract infections** |
| **SAPS** | **Simplified Acute Physiology Score** |
| **SD** | **Standard deviation** |
| **SIRS** | **Systemic inflammatory response syndrome** |
| **SOFA** | **Sequential organ failure assessment score** |

## List of Abbreviations (Cont…)

**SPSS ..... Statistical program for social science**

**TNF-α ..... Tumor necroting factor**

**VRE ..... Vancomycin-resistant Enterococcus**

**WBC ..... White Blood cell count**

**$x^2$ ..... Chi-square**

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# INTRODUCTION

The duration of antibiotic therapy in critically ill patients with sepsis is based on empirical rules ***(Calandra & Cohen, 2005),*** It can result in antibiotic overuse, increasing the risk of developing multi-drug resistant (MDR) pathogens, nosocomial superinfections and excess cost ***(Elizabeth, 2011).***

Recent attempts to decrease the duration of the antibiotic therapy have been successful in critically ill patients ***(Nobre et al., 2008).*** Patients with ventilator-associated pneumonia, were found to be equally improved when receiving an 8-day treatment compared to a 15-day course of antibiotics ***(Chastre et al., 2003).*** This is, however, again based on empirical rules. Guidance of the duration of the antibiotic treatment tailored for each patient based on simple biomarkers could contribute to an additional benefit ***(Nobre et al., 2008).***

Newer strategies aimed at identifying patients most likely to benefit from antibiotics and those that may require shorter than standard treatments using clinical biomarkers to assess presence, severity, and progression of disease like C-reactive protein (CRP), white blood cell count (WBC), interleukins (IL) and most recently, procalcitonin (PCT) has become a target tool to improve antimicrobial stewardship (***Schuetz et al., 2009).***

Procalcitonin (PCT), the biologically active precursor of the calcium-modulating hormone calcitonin ***(Meisner 2002***) has been shown in diverse studies to be closely associated with the human host response to bacterial infection ***(Castelli et al., 2004).*** It is elaborated by parenchymal cells throughout the body in response to endotoxin and several pro-inflammatory mediators (in particular TNF-α) and its concentration appears to be roughly linear with the degree of insult ***(Brunkhorst et al., 2000***). It has tantalizing characteristics as a biomarker for bacterial infection, showing diagnostic superiority to white cell count, C-reactive protein, and a host of physiologic variables in most reports ***(Wanner et al., 2000; Nobre et al., 2008).***

# AIM OF THE WORK

The study aims to evaluate the efficacy of serum procalcitonin as a biomarker in reducing the duration of antibiotics treatment in septic critically ill patients.

# SEPSIS

Sepsis which is derived from the Greek verb *sepo* (meaning "I rot") is a systemic, deleterious host response to infection leading to severe sepsis (acute organ dysfunction secondary to documented or suspected infection) and septic shock (severe sepsis plus hypotension not reversed with fluid resuscitation). Severe sepsis and septic shock are major healthcare problems, Similar to polytrauma, acute myocardial infarction, or stroke, the speed and the appropriateness of therapy administered in the initial hours after severe sepsis develops are likely to influence the outcome ***(Kaukonen et al., 2015).***

## Definitions

**Infection**: defined as a pathological process caused by the invasion of a normally sterile tissue or fluid or body cavity by pathogenic or potentially pathogenic micro-organisms. It is also important to point out that, frequently, infection is strongly suspected without being microbiologically confirmed ***(Dellinger et al., 2013)***.

**Systemic inflammatory response syndrome (SIRS**): is an inflammatory reaction that produces at least two of the following four signs:

- Abnormal body temperature: hypothermia, <96.8°F/36°C; or fever, >100.4°F/38.3°C.
- Tachycardia (>90 beats/min),
- Tachypnea (>20 breaths/min or a rate sufficient to produce $PaCO_2$ <32 mm Hg),
- Abnormal white blood cell count (>12, 000/$mm^3$, <4000/$mm^3$, or >10% immature forms) ***(Gaieski and Goyal, 2013)***.

SIRS due to abnormal white blood cell count can be triggered by an infection, but also it can arise from non-infectious sources such as trauma, haemorrhage, burns, surgery, adrenal insufficiency, pulmonary embolism, dissecting or ruptured aortic aneurysm, myocardial infarction, occult haemorrhage, cardiac tamponade, post-cardiopulmonary bypass syndrome, autoimmune disorders, pancreatitis, vasculitis, anaphylaxis, or drug overdose. SIRS can lead to organ failure, shock, and death ***(Neviere, 2013)***.

**Severe sepsis**: "sepsis syndrome, " is present when the patient has progressed to a stage in which organs or

organ systems begin to fail. Severe sepsis is sepsis plus one of the following clinical problems: Cardiovascular system dysfunction, acute respiratory distress syndrome (ARDS), dysfunction of two or more other organs or systems ***(Dellinger et al., 2013)***.

**Septic shock**: in a patient with sepsis, is an acute circulatory failure with refractory hypotension which is unexplainable by other causes. The term *shock* describes a condition in which many tissues throughout the body become hypoxic due to poor perfusion. In shock, normal homeostatic mechanisms are either not functioning or not adequate to deliver enough oxygen to tissues. If it is not reversed it leads to organ failures and death ***(Gaieski and Goyal, 2013)***.

In septic shock, there is hypotension that cannot be reversed by giving adequate fluids. When the hypotension of septic shock also does not respond to vasopressors, the condition is called *refractory septic shock* ***(Munford and Suffredini, 2009)***.

**Multiple organ dysfunction syndrome (MODS)**: failure of a number of organs or organ systems caused by an illness. To be considered "in failure" an organ must persist in its severe dysfunction for at least 24 hours ***(Dellinger et al., 2013)***.

The lack of a reliable definition of sepsis makes assessment of incidence and changes in outcomes difficult to quantify reliably leads to a new definition of sepsis ***(The Third International Consensus Definitions for Sepsis and Septic Shock (Sepsis-3))*** which recommends the following:

Sepsis should be defined as life-threatening organ dysfunction caused by a dysregulated host response to infection. For clinical operationalization, organ dysfunction can be represented by an increase in the Sequential [Sepsis-related] Organ Failure Assessment ***(SOFA)*** score of 2 points or more ***(see table 1)***, which is associated with an in-hospital mortality greater than 10 %***(Mervyn et al., 2016)***.

**Table 1:** Sequential [Sepsis-Related] Organ Failure Assessment Score ***(Mervyn et al., 2016)***.