



بسم الله الرحمن الرحيم

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Evaluation of Serum Procalcitonin as a Diagnostic and Prognostic Biomarker for Sepsis in Major Burn Patients: A Prospective Study

Thesis

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بِسْمِ اللَّهِ الرَّحْمَنِ الرَّحِيمِ

قالوا

سببنا أنك لا تعلم لنا
إلا ما علمتنا أنك أنت
العليم العظيم

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List of Contents

Title	Page No.
List of Tables	i
List of Figures.....	iii
List of Abbreviations	v
Introduction.....	1
Aim of the Work	4
Reivew of Literature	
Pathophysiology of Burn Injury	5
Sepsis in burn patients	19
Serum Procalcitonin.....	39
Patients and Methods	47
Results.....	53
Discussion.....	82
Summary.....	89
Conclusion	92
References.....	93
Arabic Summary	---

List of Tables

Table No.	Title	Page No.
Table (1):	Sepsis criteria according to ABA (American Burn Association), Mann–Salinas novel predictors of sepsis, Sepsis-3 consensus definition for sepsis and septic shock.	23
Table (2):	Guidelines for the treatment of severe sepsis and septic shock from the surviving sepsis campaign	33
Table (3):	Descriptive for demographic data and characteristics of the studied patients	53
Table (4):	Shows the distribution, depth, delay, conscious level and the outcome of the studied patients	55
Table (5):	Comparison between procalcitonin samples that had been withdrawn	58
Table (6):	Descriptive for the results of blood culture growth of the studied patients	60
Table (7):	Comparison between samples of TLC levels	63
Table (8):	Median of CRP, percentage of the bacterial growth type, sepsis and non-sepsis patients.....	64
Table (9):	Comparison between sepsis and non-sepsis cases regarding demographic data and characteristics	66
Table (10):	Comparison between sepsis and non sepsis cases regarding demographic data, outcome and procal levels	67
Table (11):	Comparison between sepsis and non sepsis cases regarding bacterial growth type	72
Table (12):	Comparison between sepsis and non sepsis regarding samples of TLC levels	73
Table (13):	Comparison between samples of CRP level and bacterial growth in sepsis and non sepsis	73

List of Tables (cont...)

Table No.	Title	Page No.
Table (14):	Descriptive for demographic data and characteristics of the studied patients regarding the outcome.....	74
Table (15):	Shows the distribution, depth, delay, conscious level and the outcome of the studied patients regarding the outcome	76
Table (16):	Comparison between survivors and non survivors cases regarding bacterial growth type.....	79
Table (17):	Comparison between samples of TLC levels regarding outcome	80
Table (18):	Comparison between samples of CRP level and bacterial growth in survivors and non survivors regarding outcome	80

List of Figures

Fig. No.	Title	Page No.
Figure (1):	Pathophysiology of burn	7
Figure (2):	Burn injury zones	9
Figure (3):	Four phases of natural wound healing	10
Figure (4):	Effect of burn injury (.....	15
Figure (5):	Events leading to sepsis and multiple organ failure following burn injury	17
Figure (6):	Differential responses at local, regional, and systemic levels.....	25
Figure (7):	A series of pathogenic events responsible for sepsis post burn injury.	26
Figure (8):	Organ Failure in Severe Sepsis and Dysfunction of the Vascular Endothelium and Mitochondria.....	29
Figure (9):	PCT production	40
Figure (10):	Procalcitonin.....	42
Figure (11):	Red top tube sample was collected	50
Figure (12):	Automated immune-analyzer (VIDAS®, bioMérieux, Marcy L'Etoile, France).....	51
Figure (13):	Demonstrates the gender distribution of the studied patients.	54
Figure (14):	Demonstrates the cause of burn of the studied patients.	54
Figure (15):	Demonstrates the burn distribution of the studied patients.	56
Figure (16):	Demonstrates the depth of burn of the studied patients.	56
Figure (17):	Demonstrates the outcome of the studied patients.	57
Figure (18):	Comparison between procalcitonin samples that had been withdrawn.	59

List of Figures (cont...)

Fig. No.	Title	Page No.
Figure (19):	Descriptive for the results of blood culture growth of the studied patients.....	61
Figure (20):	Demonstrate the blood culture bacterial organisms of the studied patients.....	62
Figure (21):	Comparison between samples of TLC levels	63
Figure (22):	Type of bacterial growth	64
Figure (23):	Percentage of sepsis patients in comparison to the non-sepsis cases.....	65
Figure (24):	Comparison between sepsis and non sepsis cases regarding distribution	68
Figure (25):	Comparison between sepsis and non sepsis cases regarding outcome.....	69
Figure (26):	Comparison between sepsis and non sepsis cases regarding procalcitonin sample 4	70
Figure (27):	Comparison between sepsis and non sepsis cases regarding procalcitonin sample 5	71
Figure (28):	Comparison between survivors and non survivors regarding the extent (%).....	75
Figure (29):	Comparison between survivors and non survivors regarding the distribution	77
Figure (30):	Comparison between survivors and non survivors regarding the procalcitonin sample 1	77
Figure (31):	Comparison between survivors and non survivors regarding the procalcitonin sample 5	78

List of Abbreviations

Abb.	Full term
<i>ABA</i>	<i>American Burn Association;</i>
<i>ARDS</i>	<i>Acute respiratory distress syndrome</i>
<i>BPM</i>	<i>Beats per minute</i>
<i>CGRP</i>	<i>Calcitonin gene-related peptide</i>
<i>DAMPs</i>	<i>Damage-associated molecular patterns</i>
<i>FiO₂</i>	<i>Fraction of inspired oxygen</i>
<i>IGF-1</i>	<i>Insulin-like growth factor 1</i>
<i>LPS</i>	<i>Lipopolysaccharide</i>
<i>MAP</i>	<i>mean arterial pressure</i>
<i>MODS</i>	<i>Multiple organ dysfunction syndrome</i>
<i>NF-κB</i>	<i>Nuclear factor kappa B</i>
<i>NOD</i>	<i>Nucleotide oligomerization domain</i>
<i>PAMPs</i>	<i>Pathogen-associated molecular pattern molecules</i>
<i>PaO₂</i>	<i>Partial pressure of arterial oxygen</i>
<i>PARs</i>	<i>Protease-activated receptors</i>
<i>PCT</i>	<i>Procalcitonin</i>
<i>qSOFA</i>	<i>Quick SOFA.</i>
<i>SIRS</i>	<i>Systemic inflammatory response syndrome</i>
<i>SOFA</i>	<i>Sequential Organ Failure Assessment</i>
<i>SPSS</i>	<i>Statistical Package for Social Science</i>
<i>TLRs</i>	<i>Toll-like receptors</i>
<i>TNF</i>	<i>Tumor necrosis factor</i>

INTRODUCTION

Sepsis in burns worsens the patient's prognosis and increases the risk of organ failure and death. The leading cause of death in burn patients is multiple organ dysfunction syndrome (MODS), which is a direct response to sepsis (*Greenhalgh, 2017*). Identifying early sepsis is very important, given that every 6 h delay in the diagnosis of sepsis reduces survival by 10%. Difficulty in diagnosing sepsis in burn is due to the systemic response to the burn itself clinically mimics sepsis (*Permatasari et al., 2021*).

Blood cultures are still the gold standard to identify sepsis, but it takes 48-72 h and cannot rapidly diagnose sepsis. In addition, because of the usage of high-dose antibiotics at an early stage, the positive detection rate of blood culture is very low, which would delay the diagnosis (*Chiesa et al., 2004*).

The currently used indicators of early diagnosis of infection like CRP are also affected greatly by many other conditions such as trauma, surgery, tissue necrosis and immune mediated inflammatory disease. Patients with severe burns do have a systemic inflammatory response, therefore, it is very important to develop new methods for differential diagnosis between a pure inflammatory reaction and a true sepsis due to microbiological invasion of the blood stream (*Barati et al., 2008*).

It is presumed that various sepsis biomarkers originating from the host response to inflammatory stimuli could diagnose sepsis as early as possible so that sepsis treatment can be started early.

Procalcitonin (PCT), a protein that consists of 116 amino acids, is a precursor of calcitonin which participates in the calcium metabolism. PCT is mainly produced by C-cells of the thyroid gland and it is also synthesized in the liver, kidneys, lungs, and adipose tissues in response to endotoxins, cytokines, and other mediators (*Xu et al., 2018*).

Under normal circumstances, healthy individuals carry very low levels of PCT. However, in the presence of bacterial and fungal infections, dramatically increased levels of PCT may be seen. Previous reviews have shown that procalcitonin (PCT) may be used as an auxiliary index in clinical diagnosis of sepsis and a modality to reduce exposure of antibiotics to critically ill patients (*Mann et al., 2011*) and may be the most promising biomarker of burn patients with sepsis (*Cabral et al., 2017*).

Studies on the evaluation of diagnostic and prognostic value of procalcitonin levels in severe burn sepsis are rare and still show inconsistent results. In 2012 *Lavrentieva* and his colleagues stated that PCT is useful as an early indicator of sepsis in severe burn patients. Meanwhile, other study showed

that PCT serum is not superior compared to CRP or blood leukocytes as a marker of sepsis in burn patients. (*Jeschke et al., 2013*)

In 2018 *Kumar* and his co-workers stated that PCT is a good sepsis marker, but different populations have difference in validity and predictability of the test. Thus, the present study was designed to find the diagnostic validity and the prognostic value of PCT in our burn population.

AIM OF THE WORK

The aim of this study is:

- To investigate the diagnostic validity of PCT in burn sepsis as an early diagnostic tool
- To identify its prognostic value in major burn patients with sepsis.

Chapter 1

PATHOPHYSIOLOGY OF BURN INJURY

Introduction

Burn injuries are an under-appreciated trauma that can affect anyone, anytime and anywhere.

The injuries can be caused by friction, cold, heat, radiation, chemical or electric sources, but the majority of burn injuries are caused by heat from hot liquids, solids or fire. Although all burn injuries involve tissue destruction due to energy transfer, different causes can be associated with different physiological and pathophysiological responses. (*Nguyen et al., 2020*).

For example, a flame or hot grease can cause an immediate deep burn, whereas scald injuries tend to appear more superficial initially, due to rapid dilution of the source and energy. Alkaline chemicals cause colliquative necrosis (whereby the tissue is transformed into a liquid, viscous mass), whereas acidic burn causes a coagulation necrosis (whereby the architecture of the dead tissue can be preserved). Electrical injuries are entirely different because they can cause deep tissue damage that is greater than the visible skin injury. (*Lee, 1997*).