Comparative study between Microalbuminuria and Simplified Acute Physiology score as a marker of mortality in septic critically ill patients

A THESIS FOR PARTIAL ULFILLMENT
OF
MASTER DEGREE IN I.C.U

By

Ahmed Mokhtar Ibrahim Hassanin
M.B.B.Ch, Faculty of Medicine, Ain Shams University

Under Supervision of

Prof. Dr. Sahar Mohammed Kamal Mahmoud Hassanin
Professor of Anesthesiology, Intensive Care and pain management
Faculty of Medicine, Ain Shams University

Dr. Mahmoud Hasan Mohamed Hasan
Assistant Professor of Anesthesiology, Intensive Care and pain management
Faculty of Medicine, Ain Shams University

Dr. Sanaa Farag Mahmoud
Lecturer of Anesthesiology, Intensive Care and pain management
Faculty of Medicine, Ain Shams University

Faculty of Medicine
Ain Shams University
2019

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List of Abbreviations

9-CM	Ninth Revision, Clinical Modification
ACCP	American College of Chest Physicians
APACHE II	Acute Physiological and Chronic Health Evaluation
APC	Antigen Presenting Cells
ARDS	Acute Respiratory Distress Syndrome
CLABSI	Central Line–Associated Bloodstream Infection
CLRs	C-Type Lectins
CVD	Cardiovascular Disease
CVP	Central Venous Pressure
DAMPs	Danger- Associated Molecular Patterns
DIC	Disseminated Intravascular Coagulation
DNA	Deoxy Ribonucleic Acid
ED	Emergency Department
EPIC	Extended Prevalence of Infection in Intensive Care
ETASS	Efficacy of Thymosin Alpha 1 for Severe Sepsis
ETC	Endothelial Cleft
GAG	Glycosaminoglycan
GBM	Glomerular Basement Membrane
GCS	Glasgow Coma Scale
GFB	Glomerular Filtration Barrier
GI	Gastro Intestinal
H3K4me3	Lysine 4 tri methylation of histone 3

H3K9me2	Dimethylation of histone 3 at lysine residue 9
H4Ac	Acetylation of histone 4
HIV	Human Immunodeficiency Virus
HLA-Dr	Human leukocyte antigen DR
HMGB-1	High-Mobility Group Box-1
HR	Heart Rate
HSPG	Heparin Sulphate Proteoglycans
ICAM-1	Intercellular Adhesion Molecule 1
ICD	International Classification of Diseases
ICU	Intensive Care Unit
ILs	Interleukins
INICC	International Nosocomial Infection Control Consortium
IV	Intravenous
LODS	Logistic Organ Dysfunction System
LOS	Length Of Stay
LPS	Lipopolysaccharide
MAP	Mean Arterial Pressure
MODS	Multiple Organ Dysfunction Score
MPM	Mortality Prediction Model
NHSN	National Healthcare Safety Network
NLRs	Nod Like Receptors
PaCO2	Arterial Carbon Dioxide Tension
PAMPs	Pathogen-Associated Molecular Patterns

Piv	Intracapillar hydrostatic pressure
PPIs	Proton Pump Inhibitors
PRR	Pattern-Recognition Receptors
QOL	Quality Of Life
RBC	Red Blood Cell
RCTs	Randomized Controlled Trials
RLRs	RIG-I Like Receptors
ROS	Reactive Oxygen Species
RR	Respiratory Rate
SAPS	Simplified Acute Physiology Score
SCCM	Society of Critical Care Medicine
ScvO2	Central Venous Oxygen Saturation
SES	Socioeconomic Status
SIRS	Systemic Inflammatory Response Syndrome
SOFA	Sequential Organ Failure Assessment
SSC	Surviving Sepsis Campaign
SVEP1	Sushi, Von Willebrand Factor Type A, Epidermal growth factor and Pentraxin domain containing 1
TF	Tissue Factor
TLR	Toll-Like Receptor
TNF	Tumor Necrosis Factor
UAE	Urine Albumin Excretion
UOP	Urine Output
UTI	Urinary Tract Infection

VAP	Ventilator-Associated Pneumonia
VCAM-1	Vascular Cell Adhesion Molecule 1
VEGF	Vascular Endothelial Growth Factor
WBC	White Blood Cell
Πis	Interstitial Colloid-Oncotic Pressure

INTRODUCTION

SEPSIS is defined as SIRS (systemic inflammatory response syndrome) that has a proven or suspected microbial etiology. Invasive bacterial infections like Non-typhoidal salmonella species, Streptococcus pneumonia, Haemophilus influenza, and Escherichia coli were the most commonly isolated bacteria and the prominent causes of death around the world. **(Routray et al., 2016)**

Sepsis is marked by severe host defense response that releases a plethora of proinflammatory molecules into the circulation. The endothelium becomes dysfunctional due to the effect of inflammatory molecules and oxidative stress. Therefore increased capillary permeability is an early feature of Systemic Inflammatory Response Syndrome (SIRS). **(Routray et al., 2016)**

Numerous markers or methods have been utilized as prognostication tools for managing such patients thereby effectively and the mortality both short- and long-term. Acute Physiology and Chronic Health Evaluation (APACHE) II and Simplified Acute Physiology Score (SAPS) II scores are two of the most commonly used methods to predict mortality but have found to be of limited value for daily practical purposes due to their complex

nature, though they have been efficient in evaluating the outcome. The measures used in ICU should ideally be sensitive, inexpensive, preferably detect short-term changes that can produce rapid and reliable results including the impact of therapeutic outcomes on the patients. **(Gagarin et al., 2012)**

In various studies microalbuminuria has been correlated with rapid changes in vascular integrity. Microalbuminuria, defined as 30–300 mg/day of albumin excretion in the urine, occurs rapidly after an acute inflammatory injury such as sepsis and persists in patients with complications. It is a common finding in critically ill patients, where it has shown promise not only as a predictor of organ failure and vasopressor requirement but also of mortality. **(Routray et al., 2016)**

A more convenient method to detect microalbuminuria is the albumin /creatinine ratio (ACR) measured in a random urine specimen. Currently, the National Kidney Foundation recommends the use of spot urine ACR obtained under standardized conditions to detect microalbuminuria. The ACR is more convenient test for patients and may be less prone to errors due to improper collection methods and variations in 24-h protein excretion compared with a random urine specimen. **(Mattix et al., 2002)**

AIM OF THE STUDY

The purpose of this study is to evaluate the relation between microalbuminuria (urine micro albumin / creatinine ratio) and SAPS II score in patients with sepsis and whether it could predict mortality in critically ill patients and to develop a simple, inexpensive and dynamic marker of critical illness.

Chapter (1):

SEPSIS

1. Definition:

A better understanding of the underlying pathobiology has been accompanied by the recognition that many existing terms (e.g. sepsis, severe sepsis) are used interchangeably, whereas others are redundant (e.g. sepsis syndrome) or overly narrow (e.g. septicemia). **(Singer et al., 2016)**

The American College of Chest Physicians (ACCP) and the Society of Critical Care Medicine (SCCM) published the first consensus definition of syndromes related to sepsis in 1992, defining the clinical criteria for systemic inflammatory response syndrome (SIRS), sepsis as SIRS in the presence of known or suspected infection, and severe sepsis and septic shock as the progression to organ dysfunction. **(Wiersinga et al., 2014)**

Since then over the last two decades, the knowledge of epidemiology of sepsis has clearly improved. No prospective studies have been performed to analyses incidence of sepsis in general population. The recent publication of the Third International Consensus Definitions for Sepsis and Septic Shock (Sepsis-3) should provide greater clarity and

consistency for future epidemiologic studies. **(Wiersinga et al., 2014)**

Sepsis is defined as life-threatening organ dysfunction caused by a dysregulated host response to infection. This new definition 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. As described later, even a modest degree of organ dysfunction when infection is first suspected is associated with in-hospital mortality in excess of 10%. Recognition of this condition thus merits a prompt and appropriate response. **(Singer et al., 2016)**

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. However, SIRS may simply reflect an appropriate host response that is frequently adaptive. Sepsis involves organ dysfunction, indicating a pathobiology more complex than infection plus an accompanying inflammatory response alone. The task force emphasis on life-threatening organ dysfunction is consistent with the view that cellular defects underlie physiologic and biochemical abnormalities within specific organ systems. Under this terminology,

"severe sepsis" becomes superfluous. Sepsis should generally warrant greater levels of monitoring and intervention, including possible admission to critical care or high-dependency facilities. **(Singer et al., 2016)**

Septic shock is defined as a subset of sepsis in which underlying circulatory, cellular, and metabolic abnormalities are associated with a greater risk of mortality than sepsis alone. Adult patients with septic shock can be identified using the clinical criteria of hypotension requiring use of vasopressors to maintain mean blood pressure of 65 mm Hg or greater and having a serum lactate level greater than 2 mmol/L persisting after adequate fluid resuscitation. **(Shankar-Hari et al.,2016)**

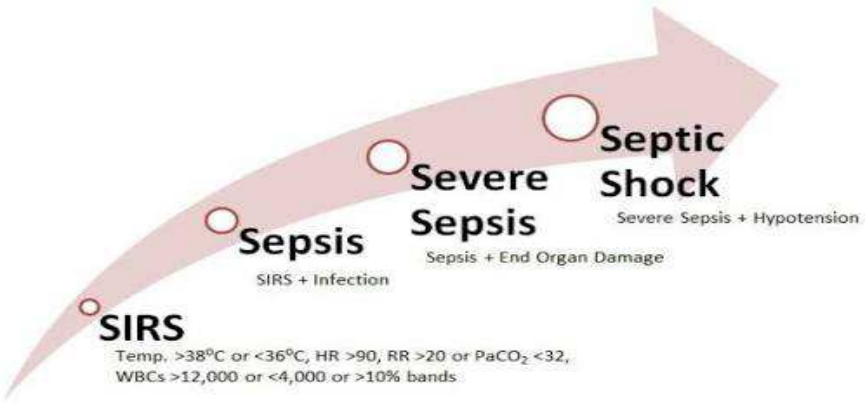

Figure (1): Stages of sepsis