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Incidence and Outcome of Sepsis in Intensive Care Unit

(in Ahmad Maher Teaching Hospital)

Thesis

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Mohammad Eltohamy

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List of Abbreviations

Abb.	Full term
ABG	Arterial blood gas
ALI	Acute lung injury
AVP	Arginine vasopressin
BBB	Blood-brain barrier
BPS	Best Practice Statement
CNS	Central nervous system
CNTF	Ciliary neurotrophic factor
COX-2	Cyclooxygenase 2
CPFA	Coupled plasma filtration adsorption
CRP	C-reactive protein
CVP	Central venous pressure
DC	Dendritic cells
DIC	Disseminated intravascular coagulation
DSI	Daily sedation interruption
DVT	Deep vein thrombosis
EGDT	Early goal-directed therapy
GI	Gastrointestinal
GM-CSF	Granulocyte-macrophage colony- stimulating factor
H_2RAs	Histamine-2 receptor antagonists
HESs	Hydroxyethyl starches
HMGB1	High mobility group box 1
ICU	Intensive Care Unit
IFN-γ	Interferon-γ
IL	Interleukin
IL-1Ra	IL-1 receptor antagonist

Abb.	Full term
LIF	Leukemia inhibitory factor
LMWH	Low-molecular-weight heparin
LOS	Length Of Stay
MAP	Mean arterial pressure
MIF	Migration inhibitory factor
MMDS	Microcirculation and Mitochondrial Distress Syndrome
NIV	Non invasive ventilation
NLR	Nucleotide-binding oligomerization domain like receptor
NMBAs	Neuromuscular blocking agents
NO	Nitric oxide
NOD	Nucleotide-oligomerization domain
OSM	Oncostatin M
PA	Pulmonary artery
PAMPs	Pathogen-associated molecular patterns
PBW	Predicted body weight
PCT	Procalcitonin
PE	Pulmonary embolism
PPIs	Proton pump inhibitors
qSOFA	Quick Sequential Organ Failure Assessment
RRT	Renal Replacement therapy
SAD	Sepsis- associated delirium
$ScvO_2$	Central venous oxygen saturation
SE	Septic encephalopathy
SIRS	Systemic inflammatory response syndrome
SOFA	Sepsis-related Organ Failure Assessment

Abb.	Full term
sTREM-1	Soluble triggering receptor expressed on myeloid cell-1
TGF-β	Transforming growth factor-β
TLR	Toll-like receptor
TNFα	Tumor necrosis factor α
UFH	Unfractionated heparin
VBG	Venous blood gas
VTE	Venous thromboembolism

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Introduction

Sepsis is the most common cause of death in non coronary intensive care units (ICUs). In the past 2 decades, the world has witnessed a significant increase in the occurrence rate of sepsis **(Zhou et al., 2017).** In ICU, sepsis may be community-acquired (e.g. already present on admission) or hospital-acquired (e.g. obtained during the ICU stay). In international prevalence studies conducted in different european countries, the rate of hospital acquired infections has varied from 3.5% to 14.8% during twenty years **(Pittet, 2005).**

Septic shock is defined as sepsis with persisting hypotension requiring vasopressors to maintain a mean arterial pressure of 65 mm Hg or higher, and blood lactate level greater than 2 mmol/l (18 mg/dl) despite adequate volume resuscitation. Diagnosis of septic shock begins with medical history and physical examination, focused on the signs and symptoms of infection, with the aim of recognizing complex physiologic manifestations of shock. Clinicians should understand the importance of prompt administration of antibiotics, vasopressors and intravenous fluids aimed at restoring adequate circulation. They should also be aware of the limitations of the protocol-based therapy **(Jacek, 2017).**

Aim of the Work

The aim of this study was to know the incidence, causes and outcome of sepsis in the intensive care unit (of Ahmad Maher Teaching Hospital, Cairo, Egypt) as a preliminary step to know and compare the incidence, causes and outcome of sepsis in different ICUs in Egypt, aiming to improve our practice.

A- Pathophysiology of Sepsis

Sepsis is a spectrum of disease, where there is systemic and a dysregulated host response to an infection. **Septic shock** is a subset of sepsis "in which circulatory, cellular, and metabolic abnormalities are associated with a greater risk of mortality than with sepsis alone. These patients can be clinically identified by a vasopressor requirement to maintain a MAP ≥ 65mmHg and serum lactate >2mmol/L in the absence of hypovolemia **(Singer et al., 2016).**

Systemic inflammatory response syndrome (SIRS) is no longer considered in defining sepsis and septic shock Instead, adult patients outside intensive care unit (ICU) with suspected infection are considered at high risk of mortality if quick sepsis-related Organ Failure Assessment (qSOFA) score is ≥ 2 (table 1) **(Singer et al., 2016).**

The Sepsis-related Organ Failure Assessment (SOFA) score is widely used in the critical care setting and is a reliable tool to distinguish septic patients. But, it requires some laboratory investigations and may be less useful for a quick screening of patients outside ICU (table 2). A simple bedside score (qSOFA) incorporates hypotension (systolic blood pressure ≤100mmHg), altered mental status and tachypnea (respiratory rate > 22/min); the

presence of at least two of these criteria strongly predicts the likelihood of poor outcome in out ICU patients with clinical suspicion of sepsis **(Singer et al., 2016).**

Table (1): Quick SOFA score

Quick SOFA Criteria	***Points***
Respiratory rate ≥22/min	1
Change in mental status	1
Systolic blood pressure ≤100 mmHg	1

qSOFA: Quick Sequential Organ Failure Assessment (SOFA) score

(Singer et al., 2016)

Risk factors for sepsis

Males are more prone than females to develop severe sepsis, although the mortality in females is higher **(Guidet and Maury, 2013)**. Elderly (over 75 years) and very young (< 1 year) patients are at increased risk. Indwelling line or catheter as well as instrumentation or surgery (including illegal abortion occurring in unhygienic circumstances) increase the risk. Other risk factors include alcohol abuse, diabetes mellitus, breach of skin integrity (e.g., burn), medications (e.g., high-dose corticosteroids and chemotherapy), immunocompromise, pregnancy and drug misuses **(Mayr et al., 2014).**

Table (2): SOFA score physiological parameters

Variables	0	1	2	3	4
PaO_2/FiO_2 mmHg	>400	<400	<300	<200 with respiratory support	<100 with respiratory support
Platelets $x10^3$ cells/uL	>150	<150	<100	<50	<20
Billirubin mg/dl	<1.2	1.2-1.9	2-5.9	6-11.9	>12.0
Hypotention	No	MAP <70mm Hg	Dopamine <5* or dobutamine any dose	Dopamine >5* or Epinephrine <0. 1* or Norepiniphrine <0.1*	Dopamine>15* or Epinephrine >0.1* or Norepinephrine >0. 1*
GCS	15	13-14	10-12	6-9	<6
Creat or UOP(ml)	<1.2	1.2-1.9	2-3.4	3.5-4.9 or <500ml	>5.0 or <200ml

(Pa_{O2}): arterial partial pressure of oxygen; (FI_{O2}): fraction of inspired oxygen GCS: glascow coma scale; Creat: creatinine; UOP: urine output; MAP: mean arterial pressure**.**

(Vincent et al., 1998)

Epidemiology

Sepsis syndrome is a major worldwide cause of morbidity and mortality; 20 - 40% of septic patients who require treatment in ICU developed sepsis outside the hospital. Sepsis occurs in approximately 2–10% of hospitalized patients, and 20–50% of critically ill patients will develop at least one episode of sepsis during their admission **(Sakr et al., 2013).**

Sepsis is the leading cause of death among critically ill patients **(Vincent et al., 2014).** It is the third most common

cause of death in the USA following heart disease and cancer, with 230,000–370,000 people dying from the disease annually **(Gaieski et al., 2013).** In addition, incidence of sepsis has been increasing every year **(Seymour et al., 2012).** A retrospective cohort study from 2000 to 2009 found that the rate of hospitalization due to sepsis increased by 11.8% / year. Similar results were obtained in Australia and New Zealand **(Kaukonen et al., 2014).**

Baharoon et al. (2015) evaluated retrospectively all admissions in a general intensive care unit in a tertiary care hospital with severe sepsis and septic shock over a period of six months. A total of 96 patients were included, which represented 15% of admissions during the study period. The mean age was 57.4 years. Sixty percent of cases were hospital-acquired infections, and 40% were community-acquired. Both carry very high mortality (58%).

The type of organism is an important determinant of outcome. Although most studies suggested an increasing incidence of gram-positive organisms, the latest European Prevalence of Infection in Intensive Care (EPIC II) study reported more gram-negative organisms (62.2% vs. 46.8). Predominant organisms were *Staphylococcus aureus*

(20.5%), *Pseudomonas* species (19.9%), *Enterobacteriacae* (mainly *E. coli*, 16.0%), fungi (19%) and *Acinetobacter* 9% (table 3) **(Mayer et al., 2014).**

Table (3): Percentage and type of organisms

Organisms	Frequency (%)
Gram-positive	**46.8**
Staphylococcus aureus	20.5
MRSA	10.2
Enterococcus	10.9
S. epidermidis	10.8
S. pneumonia	4.1
Other	6.4
Gram-negative	**62.2**
Pseudomonas species	19.9
Escherichia coli	16.0
Klebsiella	12.7
Acinetobacter species	8.8
Enterobacter	7.0
Other	17.0
Anerobes(gram-positive and gram -negative)	4.5
Fungi	**19**
Candida	17.0
Aspergillus	1.4
Other	1.0
Parasites	0.7
Other organisms	3.9

MRSA; methicillin-resistant *S. aureus*

(Mayer et al., 2014)