



Increased Body Mass Index and Adjusted Mortality in Intensive Care Unit Patients with Sepsis or Septic Shock.

Thesis

*Submitted for Partial Fulfillment of the Master Degree
IN Intensive Care Medicine*

By

Anas Abdelatty Mostafa Abdelatty
M.B., B.Ch.

Supervised by

Prof. Dr. Sherif Wadie Nashed

Professor of Anesthesia, Critical Care And Pain Management
Faculty of Medicine, Ain Shams University

Prof. Dr. Shereen Mostafa Elgengeehy

Professor of Critical Care medicine
Faculty of Medicine, Cairo University

*Faculty of medicine
Ain Shams University
2019*

بِسْمِ اللَّهِ الرَّحْمَنِ الرَّحِيمِ

قَالَ

سُبْحَانَكَ لَا عِلْمَ لَنَا
إِلَّا مَا عَلَّمْتَنَا إِنَّكَ أَنْتَ
الْعَلِيمُ الْعَظِيمُ

صدق الله العظيم

سورة البقرة الآية: ٣٢



Acknowledgement

First and foremost, I feel always indebted to Allah, the Most Kind and Most Merciful.

I'd like to express my respectful thanks and profound gratitude to Prof.dr. Sherif Wadie Nashed, Professor of Anesthesia, Critical Care And Pain Management, Faculty of Medicine, Ain Shams University, for his keen guidance, kind supervision, valuable advice and continuous encouragement, which made possible the completion of this work.

I am also delighted to express my deepest gratitude and thanks to Prof.dr. shereen mostafa Elgengeehy, Professor of Critical Care medicine, Faculty of Medicine, Cairo University for her kind care, continuous supervision, valuable instructions, constant help and great assistance throughout this work.

I would like to express my hearty thanks to all my family for their support till this work was completed.

Last but not least my sincere thanks and appreciation to all patients participated in this study.

✍ Anas Abdelatty Mostafa Abdelatty



List of Contents

<i>Title</i>	<i>Page No.</i>
List of tables	i
List of figures	iii
List of abbreviations.....	v
Introduction	1
Aim of the work	4
<u>Review of literature</u>	
Chapter (1): Obesity	5
Chapter (2): Sepsis	27
Materials and method	63
Results	69
Discussion	96
Summary	109
Conclusion.....	112
Recommendations & Limitations	113
Reference.....	114
Arabic summary	--

List of Tables

<i>Table No.</i>	<i>Title</i>	<i>Page No.</i>
Table (1):	Classification of BMI.....	9
Table (2):	Effect of obesity on multi systems	12
Table (3):	Definitions from the 1992 statement from The ACCP/SCCM Consensus	30
Table (4):	Updated Sepsis definition and criteria for diagnosis from the 2001 SCCM / ESICM / ACCP / ATS /SIS International Sepsis Definitions Conference	31
Table (5):	Diagnostic criteria for sepsis and severe sepsis. Adapted from: 2012 Surviving Sepsis Campaign Guideline	36
Table (6):	Risk factors for the three groups A, B and C (A- BMI 18-<25 & B- BMI 25 - < 30 & C- BMI > 30)	69
Table (7):	Cause of the admission in the three groups:.....	72
Table (8):	Components of APACHE II score, inflammatory markers, use of vasopressors and urine output in the three groups in the first day.....	73
Table (9):	Components of APACHE II score, inflammatory markers, use of vasopressors and urine output in the three groups in the third day:	75
Table (10):	Components of APACHE II score, inflammatory markers, use of vasopressors and urine output in the three groups in the seventh day:.....	77
Table (11):	Effect of BMI on morbidity and mortality in the three groups	78
Table (12):	Components of APACHE II score, inflammatory markers, use of vasopressors and urine output in the three groups through one week for group A	80

List of Tables

Table (13):	Components of APACHE II score, inflammatory markers, use of vasopressors and urine output in the three groups through one week for group B.....	83
Table (14):	Components of APACHE II score, inflammatory markers, use of vasopressors and urine output in the three groups through one week for group C.....	88
Table (15):	Components of APACHE II score, inflammatory markers, use of vasopressors and urine output in the three groups through one week for all the groups:.....	90

List of Figures

<i>Fig. No.</i>	<i>Title</i>	<i>Page No.</i>
Figure (1):	Silhouettes and waist circumferences representing optimal, overweight, and obese.....	7
Figure (2):	Inflammatory Responses to Sepsis.....	43
Figure (3):	Procoagulant Response in Sepsis.....	44
Figure (4):	Bar chart showing mean age for the three groups.....	70
Figure (5):	Bar chart showing the percentage between male and female in the three groups.....	70
Figure (6):	Bar chart showing the percentage of risk factors in the study groups.....	71
Figure (7):	Bar chart showing the body temperature, mean arterial pressure , heart rate and respiratory rate in the three groups in the first day.....	74
Figure (8):	Bar chart showing the use of vasopressor between the three groups.....	74
Figure (9):	Bar chart showing the arterial PH or serum HCO ₃ between the three groups.....	76
Figure (10):	Bar chart showing the level serum potassium between the three groups.....	76
Figure (11):	Bar chart showing mortality in three groups within 28 days.....	79
Figure (12):	Bar chart showing the body temperature, mean arterial pressure , heart rate and respiratory rate in the three groups in the first day.....	81
Figure (13):	Bar chart showing the level of serum sodium through one week.....	81
Figure (14):	Bar chart showing the use of vasopressor in group (A) through one week.....	82
Figure (15):	Bar chart showing the body temperature for the second group in the first week.....	84
Figure (16):	Bar chart showing the arterial PH or serum HOC ₃ for the second group in the first week.....	84
Figure (17):	Bar chart showing the Serum Potassium for the second group in the first week.....	85

Figure (18):	Bar chart showing the Hematocrit for the second group in the first week.....	85
Figure (19):	Bar chart showing the Glasgow Coma Score for the second group in the first week.....	86
Figure (20):	Bar chart showing the CRP for the second group in the first week.....	86
Figure (21):	Bar chart showing the Urine output for the second group in the first week.....	87
Figure (22):	Bar chart showing the arterial PH or Serum HCO ₃ in the third group through one week	89
Figure (23):	Bar chart showing the urine output in the third group through one week	89
Figure (24):	Bar chart showing the body temperature for the three groups in the first week.....	91
Figure (25):	Bar chart showing the mean arterial pressure for the three groups in the first week	91
Figure (26):	Bar chart showing the heart rate for the three groups in the first week	92
Figure (27):	Bar chart showing the respiratory rate for the three groups in the first week.....	92
Figure (28):	Bar chart showing the arterial PH or serum HCO ₃ for the three groups in the first week	93
Figure (29):	Bar chart showing the level of serum sodium for the three groups in the first week	93
Figure (30):	Bar chart showing the Glasgow coma score for the three groups in the first week.....	94
Figure (31):	Bar chart showing the CRP for the three groups in the first week.....	94
Figure (32):	Bar chart showing the urine output for the three groups in the first week.....	95

List of Abbreviations

<i>Abbr.</i>	<i>Full term</i>
AgRP :	Agouti-related peptide
AKI :	Acute kidney injury
APACHE:	Acute Physiology, and Chronic Health Evaluation
ARDS:	Acute respiratory distress syndrome
AT:	Antithrombin
ATP:	Adenosine triphosphate–sensitive potassium
ATS:	American Thoracic Society
BMI:	Body mass index
CART :	Cocaine- and amphetamine-regulated transcript
COPD:	Chronic obstructive pulmonary disease
CRP :	C-reactive protein
DAD:	Diffuse alveolar damage
DIC:	Disseminated intravascular coagulopathy
ED:	Emergency department
ESICM:	European Society of Intensive Care Medicine
FTO gene:	Fat mass and obesity associated gene
GCSF :	Granulocyte colony stimulating factor
GM-CSF:	Granulocyte-macrophage colony-stimulating factor
HCT :	Hematocrite
ICU:	Intensive care unit
IL-1:	Interleukin 1
LH:	lateral hypothalamus
LV :	Left ventricular

List of Abbreviations

MAP:	Mean arterial pressure
MODS:	Multiorgan dysfunction syndrome
NETs :	Neutrophil extracellular traps
NIH :	National Institutes of Health
NOS:	Nitric oxide synthase
NPY :	Neuropeptide Y
PAD:	Peripheral artery disease .
PAMPs:	Pathogen-associated molecular proteins
PARs :	Protease-activated receptors
POMC:	Pro-opiomelanocortin
qSOFA:	quick sequential organ failure assessment
SAE :	Sepsis associated encephalopathy
SBP :	Systolic blood pressure
SD:	Standard deviation
SIRS:	Systemic inflammatory response syndrome
SIS:	Surgical Infection Society
SOFA:	Sequential organ failure assessment
SSC:	Surviving Sepsis Campaign
TLRs:	Toll-like receptor family
TNF:	Tumor necrosis factor
TNF α :	Tumor necrosis factor alpha
UOP:	Urine output
VMH:	Ventromedial hypothalamus
WBC:	White blood cells
WHO:	World Health Organization

Abstract

Sepsis is life - threatening organ dysfunction caused by a dysregulated host response to infection and is characterized by the presence of suspected or proven infection accompanied by an increase in sequential (sepsis - related) organ failure assessment (SOFA) score of two points or more from baseline. Sepsis is one of the most common causes of death among hospitalized patients in the intensive care unit (ICU). It is particularly difficult to diagnose in this setting because of the multiple comorbidities and underlying diseases that these patients present. Over the past few decades, a growing body of evidence has investigated the values of different predictors of sepsis-related mortality. Previously, it was reported that old age, tachycardia, hypotension, elevated C-reactive protein (CRP) and lactate, thrombocytopenia, need of mechanical ventilation, high Acute Physiology, and Chronic Health Evaluation (APACHE) II, and high SOFA scores were variables associated with high mortality. Recently, a growing number of published studies have reported that obesity can be significantly correlate with mortality in the ICU setting. Body mass index (BMI) is one of the common clinical demographic characteristics and can be calculated from the ratio of body weight to squared height (kg/m^2). Nevertheless, data are limited regarding the role of BMI in predicting short-term mortality among patients with sepsis. Therefore, we conducted the present prospective study in order to evaluate the effect of increased BMI on mortality in ICU patients with sepsis or septic shock. The present study included 45 adult patients (≥ 16 years old) who were admitted to the ICU and treated for sepsis, severe sepsis, or septic shock. The patients were divided into three groups based on their BMI. In the present study, the average age of the included patients ranged from 55-70 years old; while the majority of patients were males. Moreover, we found that patients with a BMI $< 25\text{kg/m}^2$ were older than other groups of patients. On the other hand, patients with BMI $> 30\text{kg/m}^2$ were more likely to have diabetes mellitus. Regarding the cause of admission, our analysis showed that patients with low BMI ($< 25\text{ kg/m}^2$) were more likely to have chest infection; while patients with high BMI ($>30\text{ kg/m}^2$) were more likely to have bed sores. In terms of vital signs of the included patients during the first day of admission, the present study shows that obese patients had significantly lower body temperature, heart rate, and respiratory rates; while they had significantly higher mean arterial blood pressure than patients in other BMI groups. Our analysis showed that the mortality rate was significantly lower in obese patients than other BMI groups ($p = 0.049$). On the other hand, there were no significant associations between BMI and ICU length of stay, APACHE II Score, SOFA score, or rate of readmission. In conclusion, Obesity is a potential predictive characteristics for mortality among septic patients admitted to ICU.

Keywords: Body Mass; Index; Adjusted Mortality; Intensive Care Unit; Patients; Sepsis; Septic Shock

INTRODUCTION

BMI is a value derived from the mass (weight) and height of an individual. The BMI is defined as the body mass divided by the square of the body height, and is universally expressed in units of kg/m^2 , resulting from mass in kilograms and height in metres. - **Sepsis** is life-threatening organ dysfunction caused by a dysregulated host response to infection.

Septic shock is subset of sepsis in which circulatory, cellular, and metabolic abnormalities are associated with a greater risk of mortality than with sepsis alone . Over the last few decades, obesity has emerged as an international public health problem and is a leading cause of preventable deaths. The World Health Organization estimated in 2008 that 11% of adults aged 20 years and older were obese (body mass index [BMI] $> 30\text{kg/m}^2$) . This is of particular concern because obesity is associated with a heightened risk of morbidity and mortality from many acute and chronic medical conditions (*Honiden S, McArdle JR 2009*).

Furthermore, the prevalence of obesity is increasing across the globe , a finding that has major implications for healthcare planners and policy makers when considering

appropriate allocation of resources. Obese individuals have a greater burden of comorbid conditions than their non-obese counterparts. They also are more likely to develop physiologic derangements and have diminished physiologic reserve available to compensate for the stress of critical illness . (*Porhomayon J et al ., 2014*)

Despite these factors, investigations have been unable to conclusively demonstrate an adverse effect of obesity on outcomes from critical illness .In fact, some have suggested a protective effect of obesity, a phenomenon termed the obesity-survival paradox (*Pickkers P et al ., 2013*)

Similarly, although some studies have reported an increased risk of acquiring denovo infection in obese patients admitted to the ICU , others were unable to validate this finding „In studies of adults admitted to the ICU with sepsis, severe sepsis, or septic shock and which adjusted for other baseline variables, patients with overweight or obese BMIs, but not morbidly obese ones, had reductions in mortality at up to 28 days compared to those with normal BMIs. There are several plausible biologic and physiologic reasons for these mortality reductions with the two former categories. First, increased adipose tissue is associated with increased renin-angiotensin system activity (*Kershaw EE, Flier JS*

2004). While this increased activity contributes to the hypertension of overweight and obese patients, it could also have protective hemodynamic effects during sepsis and decreased the need for fluid or vasopressor support, therapies which in excess can adversely impact outcome. (*Yealy DM et al. , 2014*) , increased lipoprotein levels and adipose tissue in patients with increased BMI may bind and inactivate lipopolysaccharide or other harmful bacterial products released during sepsis .

Third, excess adipose tissue could provide increased beneficial energy stores during the catabolic septic state (*Thompson PA, Kitchens RL 2006*)

. Finally, excess adipose tissue may have beneficial immune functions. For example, adipose tissue has been associated with increased production of both tumor necrosis factor (TNF) and soluble TNF receptor . „Studies have suggested that obesity suppresses injurious inflammatory mediator release during sepsis and sepsis-associated acute lung injury . (*Stapleton RD, Suratt BT 2014*)

AIM OF THE WORK

Perform a systematic review of adjusted all-cause mortality for overweight, obese relative to normal BMI for adults admitted to the ICU with sepsis, severe sepsis, and septic shock.