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

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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 < 25kg/m2 were older than other groups of patients. On the other hand, patients with BMI > 30kg/m2 were more likely to have diabetes mellitus. Regarding the cause of admission, our analysis showed that patients with low BMI (< 25 kg/m2) were more likely to have chest infection; while patients with high BMI (>30 kg/m2) 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 concusion, Obesity is a potential predictive characteristics for mortality among septic patients admitted to ICU.

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1. 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/m2, 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] > 30kg/m2). 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 RL2006)***. 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.

2. Materials and Methods

Study design:

Prospective observational clinical study conducted from January 2018 to august 2018.

Study population:

Patients with severe sepsis according to the definitions of sepsis surviving campaign (SSC) 2017(**Cecconi *et al.*, 2018**).

Study facility:

Intensive Care Units (ICUs) at 6th October University Hospital.

Sample Methods and Size:

ICU patients with sepsis or septic shock according to the new guidelines of sepsis 2017, The primary outcome examined is on the effect of BMI on the adjusted odds ratio of mortality, considered in the following: ICU and hospital 28-day stay, Outcomes are presented based on comparisons between patients with normal BMI (18.5 to <25 kg/m2) versus those with underweight (<18.5 kg/m2), overweight (25 to <30 kg/m2), obese (30 to <40 kg/m2), or morbidly obese (≥40 kg/m2) BMIs. The sample size was determined to be 45 patients.

Selection Criteria of the study group:

Inclusion criteria:

1- Adults patients of both sexes with age ≥16 years.

2- Patients with sepsis, severe sepsis, or septic shock. The diagnosis of sever sepsis is established according to the definitions of the Surviving sepsis campaign (SSC) 2013(**Phillip Dellinger et al., 2013**).

3- Sepsis is due to either nosocomial pneumonia or intra-abdominal sepsis.

Exclusion criteria:

1. Late septic shock at presentation with multiple organ failure.

2. APACHE II score on admission ≥25 (predicted mortality >55%).

3. Preexisting liver cirrhosis.

4. Pregnancy.

5. Patient with malignancies.

6. Age less than 18.

Patients who are diagnosed as having sepsis due to either nosocomial pneumonia or intra-abdominal sepsis; and did not meet any of the exclusion criteria were prospectively included into the study divided into three groups:

A) Control group including 15 patients.

B) Overweight group including 15 patients.

C) Obese group including 15 patients.

Data Collection:

Patients with sepsis were subjected to the following:

1) Clinical Evaluation:

History and physical examination with special emphasis on vital signs (Blood pressure, pulse, Temperature and Respiratory Rate) and Glasgow Coma Scale; which are continuously evaluated daily.

2) Routine Laboratory investigations:

- ***CBC (complete blood count)***
- ***Coagulation profile:*** PT, INR and PTT.
- ***ABGs*** (Arterial Blood Gases).

- ***Centeral Venous Oxygen Saturation.***
- ***Liver Function Tests***: ALT (Alanine aminotransferase), AST (Aspartate aminotransferase), BIL (Total bilirubin) and albumin.
- ***Kidney Function Tests:*** urea, and serum creatinine.

These routine labs were withdrawn daily.

- ***Labs specific for the study:***
- ***Lactate***
- ***CRP*** **(C-reactive protein)**

On day 1, 3, 7,10 and 14.

3) Microbiological studies:

Including cultures (sputum, blood, urine or biological fluid according to clinical suspicion) on day 1.

4) Imaging studies: required to identify the source of sepsis e.g. (abdominal CT, ultrasound and chest x-ray).

5) Clinical data:

The following data were evaluated up to a maximum follow up period of 28 days of ICU stay.

- Length of ICU stay.
- Need for and duration of mechanical ventilation (according to our protocol).
- Need for and duration of vassopresor and inotropic support.
- Need for haemodialysis.
- Final outcome:

1) Survivors:

A) Patients recovered and discharged from ICU.

B) Patients still morbid and stayed in ICU more than 28 days.

2) Non-survivors: after 24 hours after ICU admission and before the completion of the 28 days of study period.

Statistical Analysis:

Data entry, processing, and statistical analysis were carried out using MedCalc version 15.8. Frequency tables with percentages were used for categorical variables and descriptive statistics (mean ±standard deviation or median with interquartile range) were used for numerical variables. Tests of significance (Chi-square, student's t-test, or Mann Whitney's test) were used according to the normality of the data. A P-values of less than 0.05 was considered statistically significant.

3. Results

Table (1): Risk factors for the three groups A, B and C (A- BMI 18-<25 & B- BMI 25 - < 30 & C- BMI > 30)

		BMI 18 - < 25	BMI 25 - < 30	BMI >30	Test value	P-value	Sig.
		No. = 15	No. = 15	No. = 15			
Age	Mean ± SD	70.13 ± 17.61	68 ± 11.21	55.87 ± 13.22	4.365•	0.019	S
	Range	32 – 88	45 – 83	20 – 73			
Sex	Male	11 (73.3%)	11 (73.3%)	8 (53.3%)	1.800*	0.407	NS
	Female	4 (26.7%)	4 (26.7%)	7 (46.7%)			
Hypertension	Yes	11 (73.3%)	9 (60.0%)	10 (66.7%)	0.600*	0.741	NS
	No	4 (26.7%)	6 (40.0%)	5 (33.3%)			
Diabetes Mellitus	Yes	6 (40.0%)	10 (66.7%)	14 (93.3%)	9.600*	0.008	HS
	No	9 (60.0%)	5 (33.3%)	1 (6.7%)			
Smoking	Yes	10 (66.7%)	7 (46.7%)	6 (40.0%)	2.312*	0.315	NS
	No	5 (33.3%)	8 (53.3%)	9 (60.0%)			
Heart Disease	Yes	6 (40.0%)	9 (60.0%)	5 (33.3%)	2.340*	0.310	NS
	No	9 (60.0%)	6 (40.0%)	10 (66.7%)			
COPD	Yes	3 (20.0%)	2 (13.3%)	4 (26.7%)	0.833*	0.659	NS
	No	12 (80.0%)	13 (86.7%)	11 (73.3%)			
Liver disease	Yes	5 (33.3%)	8 (53.3%)	3 (20.0%)	3.685*	0.158	NS
	No	10 (66.7%)	7 (46.7%)	12 (80.0%)			
Renal disease	Yes	5 (33.3%)	4 (26.7%)	5 (33.3%)	0.207*	0.902	NS
	No	10 (66.7%)	11 (73.3%)	10 66.7%)			

- P-value > 0.05: Non significant; P-value < 0.05: Significant; P-value < 0.01: Highly significant
- *: Chi-square test; •: One Way ANOVA test

Table (2): Cause of the admission in the three groups:

Cause of admission	BMI 18-25	BMI 25-30	BMI >30	Test value*	P-value	Sig.
	No. (%)	No. (%)	No. (%)			
Chest infection	13 (86.7%)	6 (40.0%)	8 (53.3%)	7.222	0.027	S
Urinary tract infection	8 (53.3%)	6 (40.0%)	4 (26.7%)	2.222	0.329	NS
Acute kidney injury	6 (40.0%)	7 (46.7%)	3 (20.0%)	2.522	0.283	NS
Infected bed sore	1 (6.7%)	1 (6.7%)	6 (40.0%)	7.601	0.022	S
Infected wound post operative	1 (6.7%)	2 (13.3%)	2 (13.3%)	0.450	0.799	NS
Septic peritonitis	0 (0.0%)	2 (13.3%)	3 (20.0%)	3.150	0.207	NS
Septic arthritis	0 (0.0%)	2 (13.3%)	0 (0.0%)	4.186	0.123	NS
Empyema	0 (0.0%)	1 (6.7%)	0 (0.0%)	2.045	0.360	NS
Diabetic foot	0 (0.0%)	2 (13.3%)	1 (6.7%)	2.143	0.343	NS
CVS	1 (6.7%)	3 (20.0%)	0 (0.0%)	3.841	0.146	NS

- P-value > 0.05: Non significant; P-value < 0.05: Significant; P-value < 0.01: Highly significant
- *: Chi-square test

Table (3): Components of APACHE II score, inflammatory markers, use of vasopressors and urine output in the three groups in the first day

1st day		BMI 18-25 No. = 15	BMI 25-30 No. = 15	BMI >30 No. = 15	Test value	P-value	Sig.
Body temperature	Mean ± SD	38.18 ± 0.61	38.14 ± 0.86	37.51 ± 0.70	3.929•	0.027	S
	Range	36.5 – 39.2	36.8 – 40	36 – 39			
Mean Arterial Pressure	Mean ± SD	65.33 ± 12.43	76.69 ± 17.89	83.0 ± 13.33	5.470•	0.008	HS
	Range	40 – 90	50 – 110	60 – 110			
Heart rate	Mean ± SD	119.0 ± 23.57	110.47 ± 20.69	99.80 ± 14.29	3.505•	0.039	S
	Range	70 – 158	78 – 130	76 – 140			
Respiratory rate	Mean ± SD	27.4 ± 5.26	24.4 ± 4.1	22.60 ± 2.23	5.362•	0.008	HS
	Range	20 – 40	18 – 34	18 – 26			
PaO2 or A-apo2	Mean ± SD	76.26 ± 24.92	80.95 ± 22.33	64.81 ± 22.17	1.927•	0.158	NS
	Range	45 – 126	44 – 115	36 – 133			
Arterial pH or Serum HCO3	Mean ± SD	7.31 ± 0.07	7.29 ± 0.14	7.32 ± 0.11	0.164•	0.849	NS
	Range	7.18 – 7.42	6.95 – 7.48	7.1 – 7.5			
Serum Sodium	Mean ± SD	135.93 ± 6.87	137.2 ± 7.82	137.2 ± 10.99	0.105•	0.901	NS
	Range	125 – 153	121 – 151	105 – 152			
Serum Potassium	Mean ± SD	4.29 ± 0.75	4.1 ± 0.89	3.92 ± 1.06	0.636•	0.534	NS
	Range	3.1 – 5.5	3.1 – 5.8	2.2 – 5.3			
Serum Creatinine	Mean ± SD	2.83 ± 1.58	2.57± 1.44	1.43 ± 0.84	4.716•	0.014	S
	Range	0.8 – 6.3	0.8 – 6.3	0.5 – 3.3			
Hematocrit	Mean ± SD	32.19 ± 5.86	33.11 ± 6.01	32.65 ± 8.3	0.069•	0.933	NS
	Range	19.9 – 40.1	19.9 – 43	22.9 – 53			
White Blood Count	Mean ± SD	17.67 ± 7.81	19.36 ± 8.01	21.21 ± 9.25	0.670•	0.517	NS
	Range	5.9 – 36	8.8 – 42	7.5 – 40			
Glasgow Coma Score	Mean ± SD	12.6 ± 2.53	10.87 ± 2.33	11.73 ± 3.79	1.292•	0.285	NS
	Range	7 – 15	6 – 15	3 – 15			
Serum lactate	Median (IQR)	3.2 (1.2 – 6.5)	2.4 (1.2 – 4.1)	2.3 (2.1 – 4.1)	0.124≠	0.940	NS
	Range	0.6 – 8.1	0.9 – 11.6	1.2 – 9.1			
CRP	Median (IQR)	98 (66 – 221)	103 (60 – 155)	125 (56 – 198)	0.451≠	0.798	NS
	Range	23 – 296	43 – 352	29 – 312			
Use of vasopressor	Yes	10 (66.7%)	5 (33.3%)	3 (20.0%)	7.222*	0.027	S
	No	5 (33.3%)	10 (66.7%)	12 (80.0%)			
Type of vasopressor	Noradrenaline	3 (20.0%)	4 (26.7%)	5 (33.3%)	5.000*	0.758	NS
	Dopamine nephrogenic dose	0 (0.0%)	1 (6.7%)	0 (0.0%)			
	Adrenaline	0 (0.0%)	0 (0.0%)	0 (0.0%)			
	No	11 (73.3%)	9 (60.0%)	8 (53.3%)			
	Noradrenaline, dopamine nephrogenic dose	1 (6.7%)	1 (6.7%)	1 (6.7%)			
	Noradrenaline, Adrenaline	0 (0.0%)	0 (0.0%)	1 (6.7%)			
Urine outpout	Median (IQR)	1200 (1000 – 2250)	1400 (800 – 2500)	1400 (1000 – 2300)	0.683≠	0.711	NS
	Range	100 – 2800	300 – 3500	350 – 3500			

- P-value > 0.05: Non significant; P-value < 0.05: Significant; P-value < 0.01: Highly significant
- *: Chi-square test; •: One Way ANOVA test; ≠: Kruskal-Wallis test

Table (4): Components of APACHE II score, inflammatory markers, use of vasopressors and urine output in the three groups in the third day:

3rd day		BMI 18-25 No. = 15	BMI 25-30 No. = 15	BMI >30 No. = 15	Test value	P-value	Sig.
Body temperature	Mean ± SD	37.49 ± 0.95	37.54 ± 0.53	37.58 ± 0.49	0.050•	0.952	NS
	Range	35 – 38.5	37 – 38.5	36.8 – 38.5			
Mean Arterial Pressure	Mean ± SD	80.57 ± 12.53	74.71 ± 14.02	79.77 ± 15.22	0.722•	0.492	NS
	Range	66 – 106	50 – 96	50 – 106			
Heart rate	Mean ± SD	98.5 ± 18.28	101.07 ± 15.6	103.77 ± 14.74	0.352•	0.706	NS
	Range	55 – 122	59 – 121	80 – 124			
Respiratory rate	Mean ± SD	22.5 ±2.47	24.64 ± 2.9	21.92 ± 3.77	2.973•	0.063	NS
	Range	18 – 28	19 – 30	18 – 32			
PaO2 or A-apo2	Mean ± SD	84.16 ± 42.7	93.57 ± 32.41	70.92 ± 21.96	1.533•	0.229	NS
	Range	30 – 165	38 – 142	31 – 112			
Arterial pH or Serum HCO3	Mean ± SD	7.3 ± 0.11	7.36 ± 0.08	7.4 ± 0.08	4.136•	0.024	S
	Range	7.08 – 7.5	7.18 – 7.48	7.3 – 7.56			
Serum Sodium	Mean ± SD	140.57 ± 8.21	140.29 ± 8.7	138.15 ± 8.78	0.317•	0.730	NS
	Range	124 – 160	125 – 158	113 – 150			
Serum Potassium	Mean ± SD	4.31 ± 0.78	3.45 ± 0.54	4.04 ± 1.03	4.191•	0.023	S
	Range	3.3 – 5.9	2.3 – 4.2	3 – 6.2			
Serum Creatinine	Mean ± SD	2.49 ± 1.36	2.08 ± 1.41	1.94 ± 0.9	0.704•	0.501	NS
	Range	0.7 – 4.7	0.5 – 5.2	0.8 – 3.5			
Hematocrit	Mean ± SD	31.49 ± 4.54	31.09 ± 5.04	29.92 ± 8.45	0.231•	0.795	NS
	Range	21.3 – 38	22 – 38.8	14.1 – 45			
White Blood Count	Mean ± SD	17.89 ± 6.97	20.72 ± 11.82	20.9 ± 14.3	0.304•	0.739	NS
	Range	8 – 29.7	9.2 – 57.1	1.4 – 49.3			

3rd day		BMI 18-25 No. = 15	BMI 25-30 No. = 15	BMI >30 No. = 15	Test value	P-value	Sig.
Glasgow Coma Score	Mean ± SD	12.79 ± 2.81	12.07 ± 2.27	13.31 ± 2.25	0.862•	0.431	NS
	Range	6 – 15	9 – 15	9 – 15			
Serum lactate	Median (IQR)	1.95 (0.9 – 2.7)	2 (1.6 – 3.2)	2.1 (1.9 – 3.1)	0.339≠	0.844	NS
	Range	0.6 – 6.9	0.5 – 7.5	0.9 – 5.9			
CRP	Median (IQR)	107.5 (50 – 187)	105 (60 – 139)	98 (85 – 172)	0.360≠	0.835	NS
	Range	32 – 345	23 – 312	42 – 225			
Use of vasopressor	Yes	4 (28.6%)	5 (35.7%)	5 (38.5%)	0.316*	0.854	NS
	No	10 (71.4%)	9 (64.3%)	8 (61.5%)			
Type of vasopressor	Noradrenaline	4 (28.6%)	4 (28.6%)	2 (15.4%)	9.131*	0.331	NS
	Dopamine nephrogenic dose	0 (0.0%)	1 (7.1%)	0 (0.0%)			
	Adrenaline	0 (0.0%)	0 (0.0%)	0 (0.0%)			
	No	10 (71.4%)	9 (64.3%)	8 (61.5%)			
	Noradrenaline, dopamine nephrogenic dose	0 (0.0%)	0 (0.0%)	2 (15.4%)			
	Noradrenaline, Dopamine nephrogenic dose and Adrenaline	0 (0.0%)	0 (0.0%)	1 (7.7%)			
Urine outpout	Median (IQR)	2200 (1800 – 3100)	2350 (1750 – 3400)	2600 (2000 – 3700)	0.797≠	0.671	NS
	Range	0 – 4300	0 – 6000	700 – 5500			

- P-value > 0.05: Non significant; P-value < 0.05: Significant; P-value < 0.01: Highly significant
- *: Chi-square test; •: One Way ANOVA test; ≠: Kruskal-Wallis test

Table (5): Components of APACHE II score, inflammatory markers, use of vasopressors and urine output in the three groups in the seventh day:

7th day		BMI 18-25 No. = 15	BMI 25-30 No. = 15	BMI >30 No. = 15	Test value	P-value	Sig.
Body temperature	Mean ± SD	37.27 ± 0.86	37.4 ± 0.55	37.44 ± 0.49	0.214•	0.808	NS
	Range	36 – 39.7	36.9 – 38.4	36.5 – 38.2			
Mean Arterial Pressure	Mean ± SD	74.42 ± 14.51	80.5 ± 11.82	85.91 ± 12.55	2.242•	0.123	NS
	Range	45 – 94	65 – 102	70 – 106			
Heart rate	Mean ± SD	103.83 ± 12.78	98 ± 19.69	101.27 ± 9.49	0.471•	0.628	NS
	Range	87 – 132	70 – 147	82 – 120			
Respiratory rate	Mean ± SD	21.58 ± 2.47	22.5 ± 2.5	22 ± 3	0.358•	0.702	NS
	Range	18 – 28	19 – 28	18 – 26			
PaO2 or A-apo2	Mean ± SD	78.28 ± 25.36	90.88 ± 29.51	74.1 ± 18.84	1.411•	0.259	NS
	Range	29.7 – 112	36.4 – 131	39 – 101			
Arterial pH or Serum HCO3	Mean ± SD	7.37 ± 0.06	7.41 ± 0.09	7.38 ± 0.07	0.980•	0.386	NS
	Range	7.29 – 7.52	7.18 – 7.52	7.28 – 7.53			
Serum Sodium	Mean ± SD	141.17 ± 8.46	137.92 ± 6.1	139.55 ± 8.65	0.521•	0.599	NS
	Range	127 – 156	129 – 152	119 – 153			
Serum Potassium	Mean ± SD	4.05 ± 0.56	3.51 ± 0.51	4.12 ± 0.94	2.782•	0.077	NS
	Range	3.6 – 5.34	2.5 – 4.1	2.5 – 5.3			
Serum Creatinine	Mean ± SD	2.12 ± 1.11	1.63 ± 1.1	1.91 ± 0.83	0.673•	0.517	NS
	Range	0.7 – 4.2	0.7 – 4.8	1 – 3.6			
Hematocrit	Mean ± SD	31.57 ± 5.07	30.23 ± 4.47	30.71 ± 7.01	0.176•	0.839	NS
	Range	18.7 – 36.7	23.3 – 37.5	14.7 – 41			
White Blood Count	Mean ± SD	17.45 ± 8.35	18.19 ± 12.51	21.66 ± 11.77	0.474•	0.627	NS
	Range	8.1 – 33.4	8.4 – 54	9.2 – 50.7			
Glasgow Coma Score	Mean ± SD	13 ± 3.57	12.83 ± 2.41	13.82 ± 2.23	0.398•	0.675	NS
	Range	5 – 15	9 – 15	9 – 15			
Serum lactate	Median (IQR)	1.2 (1 – 1.75)	1.6 (1 – 2.35)	2 (1.6 – 3.2)	3.100≠	0.212	NS
	Range	0.6 – 5.1	0.8 – 4.2	0.8 – 4.1			
CRP	Median (IQR)	59.5 (38.5 – 132)	72.5(46.5 – 130.5)	119 (78 – 132)	3.197≠	0.202	NS
	Range	1.7 – 276	13 – 284	72 – 319			
Use of vasopressor	Yes	3 (25.0%)	3 (25.0%)	4 (36.4%)	0.477*	0.788	NS
	No	9 (75.0%)	9 (75.0%)	7 (63.6%)			
Type of vasopressor	Noradrenaline	3 (25.0%)	2 (16.7%)	2 (18.2%)	6.652*	0.354	NS
	Dopamine nephrogenic dose	0 (0.0%)	0 (0.0%)	0 (0.0%)			
	Adrenaline	0 (0.0%)	0 (0.0%)	0 (0.0%)			
	No	9 (75.0%)	9 (75.0%)	7 (63.6%)			
	Noradrenaline, dopamine nephrogenic dose	0 (0.0%)	0 (0.0%)	2 (18.2%)			
	Noradrenaline, Adrenaline	0 (0.0%)	1 (8.3%)	0 (0.0%)			
Urine outpout	Median (IQR)	2100 (1775 – 2700)	2675 (1725 – 3050)	2700 (1800 – 4700)	2.267≠	0.322	NS
	Range	1200 – 3400	1250 – 3500	1550 – 6200			

- P-value > 0.05: Non significant; P-value < 0.05: Significant; P-value < 0.01: Highly significant
- *: Chi-square test; •: One Way ANOVA test; ≠: Kruskal-Wallis test

Table (6): Effect of BMI on morbidity and mortality in the three groups

		BMI 18-25	BMI 25-30	BMI >30	Test value	P-value	Sig.
		No. = 15	No. = 15	No. = 15			
Age points	Mean ± SD	4.53 ± 2.2	4 ± 2.07	2.93 ± 1.49	2.635•	0.084	NS
	Range	0 – 6	0 – 6	0 – 5			
Chronic Health Points	Median (IQR)	0 (0 – 0)	0 (0 – 5)	0 (0 – 5)	0.235≠	0.889	NS
	Range	0 – 5	0 – 5	0 – 5			
Total APACHE II Score	Mean ± SD	20.67 ± 7.19	23.33 ± 6.98	20.73 ± 7.5	0.665•	0.520	NS
	Range	8 – 34	11 – 38	11 – 36			
Total sofa Score	Mean ± SD	7.47 ± 2.95	9.27 ± 3.88	7.53 ± 3.4	1.327•	0.276	NS
	Range	2 – 12	2 – 15	2 – 15			
Days of ICU stay	Mean ± SD	11 ± 4.96	11.33 ± 4.73	12.67 ± 7.06	0.362•	0.699	NS
	Range	3 – 22	3 – 19	2 – 26			
Readmition to ICU	Yes	1 (6.7%)	0 (0.0%)	0 (0.0%)	2.045*	0.360	NS
	No	14 (93.3%)	15 (100.0%)	15 (100.0%)			
Mortality within 28days	Yes	9 (60.0%)	4 (26.7%)	3 (20.0%)	6.013*	0.049	S
	No	6 (40.0%)	11 (73.3%)	12 (80.0%)			

- P-value > 0.05: Non significant; P-value < 0.05: Significant; P-value < 0.01: Highly significant *: Chi-square test; •: One Way ANOVA test; ≠: Kruskal-Wallis test

Table (1): Components of APACHE II score, inflammatory markers, use of vasopressors and urine output in the three groups through one week for group A:

		BMI 18-25			Test value	P-value	Sig.
		1st day	3rd day	7th day			
Body temperature	Mean ± SD	38.18 ± 0.61	37.49 ± 0.95	37.27 ± 0.86	3.757•	0.044	S
	Range	36.5 – 39.2	35 – 38.5	36 – 39.7			
Mean Arterial Pressure	Mean ± SD	65.33 ± 12.43	80.57 ± 12.53	74.42 ± 14.51	3.859•	0.042	S
	Range	40 – 90	66 – 106	45 – 94			
Heart rate	Mean ± SD	119.0 ± 23.57	98.5 ± 18.28	103.83 ± 12.78	4.202•	0.019	S
	Range	70 – 158	55 – 122	87 – 132			
Respiratory rate	Mean ± SD	27.4 ± 5.26	22.5 ±2.47	21.58 ± 2.47	5.974•	0.007	HS
	Range	20 – 40	18 – 28	18 – 28			
PaO2 or A-apo2	Mean ± SD	76.26 ± 24.92	84.16 ± 42.7	78.28 ± 25.36	0.063•	0.926	NS
	Range	45 – 126	30 – 165	29.7 – 112			
Arterial pH or Serum HCO3	Mean ± SD	7.31 ± 0.07	7.3 ± 0.11	7.37 ± 0.06	2.599•	0.107	NS
	Range	7.18 – 7.42	7.08 – 7.5	7.29 – 7.52			
Serum Sodium	Mean ± SD	135.93 ± 6.87	140.57 ± 8.21	141.17 ± 8.46	7.324•	0.007	HS
	Range	125 – 153	124 – 160	127 – 156			
Serum Potassium	Mean ± SD	4.29 ± 0.75	4.31 ± 0.78	4.05 ± 0.56	2.428•	0.119	NS
	Range	3.1 – 5.5	3.3 – 5.9	3.6 – 5.34			
Serum Creatinine	Mean ± SD	2.83 ± 1.58	2.49 ± 1.36	2.12 ± 1.11	4.211•	0.012	S
	Range	0.8 – 6.3	0.7 – 4.7	0.7 – 4.2			
Hematocrit	Mean ± SD	32.19 ± 5.86	31.49 ± 4.54	31.57 ± 5.07	0.021•	0.969	NS
	Range	19.9 – 40.1	21.3 – 38	18.7 – 36.7			
White Blood Count	Mean ± SD	17.67 ± 7.81	17.89 ± 6.97	17.45 ± 8.35	0.548•	0.562	NS
	Range	5.9 – 36	8 – 29.7	8.1 – 33.4			
Glasgow Coma Score	Mean ± SD	12.6 ± 2.53	12.79 ± 2.81	13 ± 3.57	0.040•	0.884	NS
	Range	7 – 15	6 – 15	5 – 15			
Serum lactate	Median (IQR)	3.2 (1.2 – 6.5)	1.95 (0.9 – 2.7)	1.2 (1 – 1.75)	5.167≠	0.076	NS
	Range	0.6 – 8.1	0.6 – 6.9	0.6 – 5.1			
CRP	Median (IQR)	98 (66 – 221)	107.5 (50 – 187)	59.5 (38.5 – 132)	0.667≠	0.717	NS
	Range	23 – 296	32 – 345	1.7 – 276			
Use of vasopressor	Yes	10 (66.7%)	4 (28.6%)	3 (25.0%)	6.224*	0.044	NS
	No	5 (33.3%)	10 (71.4%)	9 (75.0%)			
Type of vasopressor	Noradrenaline	3 (20.0%)	4 (28.6%)	3 (25.0%)	1.965*	0.999	NS
	Dopamine nephrogenic dose	0 (0.0%)	0 (0.0%)	0 (0.0%)			
	Adrenaline	0 (0.0%)	0 (0.0%)	0 (0.0%)			
	No	11 (73.3%)	10 (71.4%)	9 (75.0%)			
	Noradrenaline, dopamine nephrogenic dose	1 (6.7%)	0 (0.0%)	0 (0.0%)			
	Noradrenaline, Adrenaline	0 (0.0%)	0 (0.0%)	0 (0.0%)			
	Noradrenaline, Dopamine nephrogenic dose and Adrenaline	0 (0.0%)	0 (0.0%)	0 (0.0%)			
Urine outpout	Median (IQR)	1200 (1000 – 2250)	2200 (1800 – 3100)	2100 (1775 – 2700)	4.667≠	0.097	NS
	Range	100 – 2800	0 – 4300	1200 – 3400			

- P-value > 0.05: Non significant; P-value < 0.05: Significant; P-value < 0.01: Highly significant
- *: Chi-square test; •: Repeated measures ANOVA test; ≠: Fried man test

Table (8): Components of APACHE II score, inflammatory markers, use of vasopressors and urine output in the three groups through one week for group B:

		BMI 25-30			Test value	P-value	Sig.
		1st day	3rd day	7th day			
Body temperature	Mean ± SD	38.14 ± 0.86	37.54 ± 0.53	37.4 ± 0.55	11.741	0.000	HS
	Range	36.8 – 40	37 – 38.5	36.9 – 38.4			
Mean Arterial Pressure	Mean ± SD	76.69 ± 17.89	74.71 ± 14.02	80.5 ± 11.82	0.671	0.475	NS
	Range	50 – 110	50 – 96	65 – 102			
Heart rate	Mean ± SD	110.47 ± 20.69	101.07 ± 15.6	98 ± 19.69	1.058	0.363	NS
	Range	78 – 130	59 – 121	70 – 147			
Respiratory rate	Mean ± SD	24.4 ± 4.1	24.64 ± 2.9	22.5 ± 2.5	1.669	0.215	NS
	Range	18 – 34	19 – 30	19 – 28			
PaO2 or A-apo2	Mean ± SD	80.95 ± 22.33	93.57 ± 32.41	90.88 ± 29.51	0.995	0.385	NS
	Range	44 – 115	38 – 142	36.4 – 131			
Arterial pH or Serum HCO3	Mean ± SD	7.29 ± 0.14	7.36 ± 0.08	7.41 ± 0.09	4.625	0.025	S
	Range	6.95 – 7.48	7.18 – 7.48	7.18 – 7.52			
Serum Sodium	Mean ± SD	137.2 ± 7.82	140.29 ± 8.7	137.92 ± 6.1	1.448	0.258	NS
	Range	121 – 151	125 – 158	129 – 152			
Serum Potassium	Mean ± SD	4.1 ± 0.89	3.45 ± 0.54	3.51 ± 0.51	5.301	0.023	S
	Range	3.1 – 5.8	2.3 – 4.2	2.5 – 4.1			
Serum Creatinine	Mean ± SD	2.57± 1.44	2.08 ± 1.41	1.63 ± 1.1	1.983	0.184	NS
	Range	0.8 – 6.3	0.5 – 5.2	0.7 – 4.8			
Hematocrit	Mean ± SD	33.11 ± 6.01	31.09 ± 5.04	30.23 ± 4.47	5.361	0.025	S
	Range	19.9 – 43	22 – 38.8	23.3 – 37.5			
White Blood Count	Mean ± SD	19.36 ± 8.01	20.72 ± 11.82	18.19 ± 12.51	0.773	0.414	NS
	Range	8.8 – 42	9.2 – 57.1	8.4 – 54			
Glasgow Coma Score	Mean ± SD	10.87 ± 2.33	12.07 ± 2.27	12.83 ± 2.41	7.178	0.011	S
	Range	6 – 15	9 – 15	9 – 15			
Serum lactate	Median (IQR)	2.4 (1.2 – 4.1)	2 (1.6 – 3.2)	1.6 (1 – 2.35)	3.957	0.138	NS
	Range	0.9 – 11.6	0.5 – 7.5	0.8 – 4.2			
CRP	Median (IQR)	103 (60 – 155)	105 (60 – 139)	72.5(46.5 – 130.5)	6.167	0.046	S
	Range	43 – 352	23 – 312	13 – 284			
Use of vasopressor	Yes	5 (33.3%)	5 (35.7%)	3 (25.0%)	0.371	0.830	NS
	No	10 (66.7%)	9 (64.3%)	9 (75.0%)			
Type of vasopressor	Noradrenaline	4 (26.7%)	4 (28.6%)	2 (16.7%)	5.642	0.933	NS
	Dopamine nephrogenic dose	1 (6.7%)	1 (7.1%)	0 (0.0%)			
	Adrenaline	0 (0.0%)	0 (0.0%)	0 (0.0%)			
	No	9 (60.0%)	9 (64.3%)	9 (75.0%)			
	Noradrenaline, dopamine nephrogenic dose	1 (6.7%)	0 (0.0%)	0 (0.0%)			
	Noradrenaline, Adrenaline	0 (0.0%)	0 (0.0%)	1 (8.3%)			
	Noradrenaline, Dopamine nephrogenic dose and Adrenaline	0 (0.0%)	0 (0.0%)	0 (0.0%)			
Urine outpout	Median (IQR)	1400 (800 – 2500)	2350 (1750 – 3400)	2675 (1725 – 3050)	9.319	0.009	HS
	Range	300 – 3500	0 – 6000	1250 – 3500			

- P-value > 0.05: Non significant; P-value < 0.05: Significant; P-value < 0.01: Highly significant
- *: Chi-square test; •: Repeated measures ANOVA test; ≠: Fried man test

Table (2): Components of APACHE II score, inflammatory markers, use of vasopressors and urine output in the three groups through one week for group C:

		BMI >30			Test value	P-value	Sig.
		1st day	3rd day	7th day			
Body temperature	Mean ± SD	37.51 ± 0.70	37.58 ± 0.49	37.44 ± 0.49	0.736•	0.442	NS
	Range	36 – 39	36.8 – 38.5	36.5 – 38.2			
Mean Arterial Pressure	Mean ± SD	83.0 ± 13.33	79.77 ± 15.22	85.91 ± 12.55	0.370•	0.593	NS
	Range	60 – 110	50 – 106	70 – 106			
Heart rate	Mean ± SD	99.80 ± 14.29	103.77 ± 14.74	101.27 ± 9.49	0.103•	0.902	NS
	Range	76 – 140	80 – 124	82 – 120			
Respiratory rate	Mean ± SD	22.60 ± 2.23	21.92 ± 3.77	22 ± 3	0.083•	0.901	NS
	Range	18 – 26	18 – 32	18 – 26			
PaO2 or A-apo2	Mean ± SD	64.81 ± 22.17	70.92 ± 21.96	74.1 ± 18.84	0.672•	0.475	NS
	Range	36 – 133	31 – 112	39 – 101			
Arterial pH or Serum HCO3	Mean ± SD	7.32 ± 0.11	7.4 ± 0.08	7.38 ± 0.07	5.238•	0.017	S
	Range	7.1 – 7.5	7.3 – 7.56	7.28 – 7.53			
Serum Sodium	Mean ± SD	137.2 ± 10.99	138.15 ± 8.78	139.55 ± 8.65	1.862•	0.200	NS
	Range	105 – 152	113 – 150	119 – 153			
Serum Potassium	Mean ± SD	3.92 ± 1.06	4.04 ± 1.03	4.12 ± 0.94	1.066•	0.355	NS
	Range	2.2 – 5.3	3 – 6.2	2.5 – 5.3			
Serum Creatinine	Mean ± SD	1.43 ± 0.84	1.94 ± 0.9	1.91 ± 0.83	3.516•	0.079	NS
	Range	0.5 – 3.3	0.8 – 3.5	1 – 3.6			
Hematocrit	Mean ± SD	32.65 ± 8.3	29.92 ± 8.45	30.71 ± 7.01	1.234•	0.311	NS
	Range	22.9 – 53	14.1 – 45	14.7 – 41			

		BMI >30			Test value	P-value	Sig.
		1st day	3rd day	7th day			
White Blood Count	Mean ± SD	21.21 ± 9.25	20.9 ± 14.3	21.66 ± 11.77	0.258•	0.773	NS
	Range	7.5 – 40	1.4 – 49.3	9.2 – 50.7			
Glasgow Coma Score	Mean ± SD	11.73 ± 3.79	13.31 ± 2.25	13.82 ± 2.23	2.326•	0.155	NS
	Range	3 – 15	9 – 15	9 – 15			
Serum lactate	Median (IQR)	2.3 (2.1 – 4.1)	2.1 (1.9 – 3.1)	2 (1.6 – 3.2)	2.905≠	0.234	NS
	Range	1.2 – 9.1	0.9 – 5.9	0.8 – 4.1			
CRP	Median (IQR)	125 (56 – 198)	98 (85 – 172)	119 (78 – 132)	0.182≠	0.913	NS
	Range	29 – 312	42 – 225	72 – 319			
Use of vasopressor	Yes	3 (20.0%)	5 (38.5%)	4 (36.4%)	1.339*	0.512	NS
	No	12 (80.0%)	8 (61.5%)	7 (63.6%)			
Type of vasopressor	Noradrenaline	5 (33.3%)	2 (15.4%)	2 (18.2%)	5.624*	0.934	NS
	Dopamine nephrogenic dose	0 (0.0%)	0 (0.0%)	0 (0.0%)			
	Adrenaline	0 (0.0%)	0 (0.0%)	0 (0.0%)			
	No	8 (53.3%)	8 (61.5%)	7 (63.6%)			
	Noradrenaline, dopamine nephrogenic dose	1 (6.7%)	2 (15.4%)	2 (18.2%)			
	Noradrenaline, Adrenaline	1 (6.7%)	0 (0.0%)	0 (0.0%)			
	Noradrenaline, Dopamine nephrogenic dose and Adrenaline	0 (0.0%)	1 (7.7%)	0 (0.0%)			
Urine outpout	Median (IQR)	1400 (1000 – 2300)	2600 (2000 – 3700)	2700 (1800 – 4700)	10.093≠	0.006	HS
	Range	350 – 3500	700 – 5500	1550 – 6200			

- P-value > 0.05: Non significant; P-value < 0.05: Significant; P-value < 0.01: Highly significant
- *: Chi-square test; •: Repeated measures ANOVA test; ≠: Fried man test

Table (10): Components of APACHE II score, inflammatory markers, use of vasopressors and urine output in the three groups through one week for all the groups:

		All cases			Test value	P-value	Sig.
		1st day	3rd day	7th day			
Body temperature	Mean ± SD	37.94 ± 0.78	37.53 ± 0.68	37.37 ± 0.64	9.489•	0.000	HS
	Range	36 – 40	35 – 38.5	36 – 39.7			
Mean Arterial Pressure	Mean ± SD	74.74 ± 16.11	78.32 ± 13.83	80.11 ± 13.49	4.092•	0.028	S
	Range	40 – 110	50 – 106	45 – 106			
Heart rate	Mean ± SD	109.76 ± 21.0	101.05 ± 16.05	101.03 ± 14.52	3.720•	0.032	S
	Range	70 – 158	55 – 124	70 – 147			
Respiratory rate	Mean ± SD	24.80 ± 4.44	23.05 ± 3.22	22.03 ± 2.61	4.612•	0.021	S
	Range	18 – 40	18 – 32	18 – 28			
PaO2 or A-apo2	Mean ± SD	74.01 ± 23.66	83.17 ± 34.14	81.29 ± 25.43	1.042•	0.356	NS
	Range	36 – 133	30 – 165	29.7 – 131			
Arterial pH or Serum HCO3	Mean ± SD	7.31 ± 0.11	7.35 ± 0.1	7.38 ± 0.07	6.540•	0.003	HS
	Range	6.95 – 7.5	7.08 – 7.56	7.18 – 7.53			
Serum Sodium	Mean ± SD	136.78 ± 8.56	139.71 ± 8.42	139.54 ± 7.69	6.979•	0.003	HS
	Range	105 – 153	113 – 160	119 – 156			
Serum Potassium	Mean ± SD	4.1 ± 0.9	3.93 ± 0.87	3.89 ± 0.72	1.891•	0.167	NS
	Range	2.2 – 5.8	2.3 – 6.2	2.5 – 5.34			
Serum Creatinine	Mean ± SD	2.28 ± 1.43	2.17 ± 1.24	1.89 ± 1.02	1.289•	0.275	NS
	Range	0.5 – 6.3	0.5 – 5.2	0.7 – 4.8			
Hematocrit	Mean ± SD	32.65 ± 6.67	30.86 ± 6.07	30.84 ± 5.43	1.726•	0.187	NS
	Range	19.9 – 53	14.1 – 45	14.7 – 41			
White Blood Count	Mean ± SD	19.41 ± 8.32	19.81 ± 11.16	19.03 ± 10.83	0.386•	0.664	NS
	Range	5.9 – 42	1.4 – 57.1	8.1 – 54			
Glasgow Coma Score	Mean ± SD	11.73 ± 2.97	12.71 ± 2.45	13.2 ± 2.76	4.396•	0.024	S
	Range	3 – 15	6 – 15	5 – 15			
Serum lactate	Median (IQR)	2.6 (1.3 – 4.1)	2.1 (1.6 – 3.1)	1.6 (1.1 – 2.5)	10.788≠	0.005	HS
	Range	0.6 – 11.6	0.5 – 7.5	0.6 – 5.1			
CRP	Median (IQR)	103 (65 – 192)	103 (56 – 172)	81 (55 – 132)	3.486≠	0.175	NS
	Range	23 – 352	23 – 345	1.7 – 319			
Use of vasopressor	Yes	17 (37.8%)	14 (34.1%)	10 (28.6%)	0.747*	0.688	NS
	No	28 (62.2%)	27 (65.9%)	25 (71.4%)			
Type of vasopressor	Noradrenaline	12 (26.7%)	10 (24.4%)	7 (20.0%)	4.586*	0.970	NS
	Dopamine nephrogenic dose	1 (2.2%)	1 (2.4%)	0 (0.0%)			
	Adrenaline	0 (0.0%)	0 (0.0%)	0 (0.0%)			
	No	28 (62.2%)	27 (65.9%)	25 (71.4%)			
	Noradrenaline, dopamine nephrogenic dose	3 (6.7%)	2 (4.9%)	2 (5.7%)			
	Noradrenaline, Adrenaline	1 (2.2%)	0 (0.0%)	1 (2.9%)			
	Noradrenaline, Dopamine nephrogenic dose and Adrenaline	0 (0.0%)	1 (2.4%)	0 (0.0%)			
Urine outpout	Median (IQR)	1400 (1000 – 2250)	2350 (1800 – 3300)	2600 (1800 – 3000)	23.232≠	0.000	HS
	Range	100 – 3500	0 – 6000	1200 – 6200			

- P-value > 0.05: Non significant; P-value < 0.05: Significant; P-value < 0.01: Highly significant
- *: Chi-square test; •: Repeated measures ANOVA test; ≠: Fried man test

4. Discussion

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(**Singer et al., 2016**).

According to previous epidemiological figures, the in-hospital mortality data among septic patients remains remarkably high and worse mortality data are reported at 1 and 5 years posthospitalization with septic patients. The odds of death varied by age. it is estimated that sepsis affects around 1.5 million individuals in the United States annually, causing the death of 250,000 individuals and being responsible for 1 out of every 3 hospital deaths. Giving this high mortality burden of sepsis, information regarding early predictive factors for mortality and morbidity are required to improve patients outcomes(**Hajj et al., 2018**).

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(**Mohamed et al., 2017**).

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). According to the definition of the National Institutes of Health (NIH), obesity can be classified into different categories on the basis of BMI: overweight (BMI ≥25 to <30 kg/m^2), obese (BMI ≥30 to <40 kg/m^2), or morbidly obese (BMI ≥40 kg/m^2), compared to normal weight (BMI ≥18.5 < 25 kg/m^2) and underweight (BMI <18.5 kg/m^2)(**Akram et al., 2000**). Previously, it was reported that BMI <18.5 kg/m^2 is a possible screening variable for malnutrition and that low BMI is associated with increased mortality in Western and Asian patient groups(**Compher et al., 2018**).

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.

There is a wide range of risk factors for severe sepsis which can broadly be divided into risk factors for infection and, contingent upon developing an infection, risk factors for organ dysfunction. Both old age and male gender, are important risk factors for severe sepsis. The incidence of severe sepsis increases disproportionately in older adults, and more than half of severe sepsis cases occur in adults over 65 years of age(**Mayr et al., 2014**). 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 < 25kg/m2 were older than other groups of patients. On the other hand, patients with BMI > 30kg/m2 were more likely to have diabetes mellitus.

The current body of evidence shows that the mean age decreased linearly with an increase in BMI category. In agreement with our findings, (**Nagai and colleagues 2010**) performed a nation-wide survey study to clarify the effect of age on the association between BMI and all-cause mortality. A total of 43 972 Japanese participants aged 40 to 79 years were followed-up for 12 years. The results showed thatpatients with BMI < 18 and between 28-25 kg/m2 were significantly older than other groups of patients.

On the other hand, obesity is the main risk factor for diabetes; increases in body weight have resulted in an increasing number of diabetic cases being diagnosed(**Bhupathiraju & Hu, 2016**). Similar to our findings, (**Wang and colleagues 2016**) performedcross-sectional study to compare the associations between different obesity indices and T2DM for middle-aged and elderly people from six communities in Jinan, China in 2011–2012. A total of 3277 residents aged ≥50 years were eligible for this study. The results showed that obese individuals were more likely to have diabetes than other BMI groups.

Respiratory tract infections, particularly pneumonia, are the most common site of infection and associated with the highest mortality. Men and alcoholics are particularly prone to developing pneumonia, while genitourinary infections are more common among women. Other common sources of infection include abdominal, skin, and soft tissue,

device-related, central nervous system, and endocarditis(**Mayr et al., 2010**).

Regarding the cause of admission, our analysis showed that patients with low BMI (< 25 kg/m2) were more likely to have chest infection; while patients with high BMI (>30 kg/m2) were more likely to have bed sores.

Similar to our findings, **(Wacharasint and colleagues 2013)** performeda retrospective analysis comparing three groups of septic shock patients based on the intervals of BMI in patients enrolled in the VASST (Vasopressin and Septic Shock Trial) cohort. Of the 778 patients in VASST, 730 patients who had body weight and height measurements were analyzed. Compared to the patients with BMI <25 kg/m^2, obese and overweight patients had a different pattern of infection with less lung and fungal infection.

Additionally, **(Arabi and colleagues 2013)** performed a nested cohort study within a retrospective database of patients with septic shock conducted in 28 medical centers in Canada, the United States, and Saudi Arabia between 1996 and 2008. Of the 8,670 patients with septic shock, 2,882 (33.2%) had height and weight data recorded at ICU admission and constituted the study group. Obese patients were more likely to have skin and soft tissue infections and less likely to have pneumonia with predominantly Gram-positive microorganisms.

The exact mechanisms of the association between weight and pattern of infection remain unclear. Large epidemiological studies have studied the potential association between obesity and increased pneumonia risk showing controversial results(**Huttunen & Syrjänen**, **2013**). Thus, further studies are still needed to elaborate this association.

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.

These findings can be explained by the fact thatlack of physical activity is reported to be associated with hypertension, while obese patients were less likely to have adequate physical activity demonstrating a significant correlation between body weight and blood pressure (**Strasser et al., 2015**). On the other hand, obesity is generally associated with a reduced core body temperature which can explain the lower temperature observed in our study among obese patients (**Heikens et al., 2011**).

It has been recently postulated that underweight and obese patients with septic shock had fewer hemodynamic disturbances and, thus, required lower doses of vasopressors (expressed as mcg/kg/minute for norepinephrine and epinephrine) than normal-weight patients, although with comparable APACHE II scores(**Arabi et al., 2013**).In the present study, fewer patients with BMI > 30 kg/m2 required the use of vasopressors than patients in other BMI groups.

In agreement with our findings, (**Wacharasint and colleagues 2013**) found that patients with BMI >30 kg/m^2 were less likely to require the administration of vasopressors. A similar finding was observed by **(Arabi and colleagues 2013**) study.

As mentioned before, sepsis is a common cause of death or significant morbidity in the ICU setting, while BMI can have a potential role in the outcomes of sepsis. The primary outcome of the present study was to assess the association between BMI and 28 days mortality, 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 concordance with our findings, (**Kuperman and colleagues 2013**) performeda retrospective chart review of patients admitted with a primary billing diagnosis of sepsis at a single United States university hospital from 2007 to 2010. Seven hundred and ninety-two charts were identified meeting the inclusion criteria. The results showed that survivors had higher average BMI than nonsurvivors (p = 0.03) in unadjusted analysis. On the other hand, the Severity of illness and comorbid conditions were similar across BMI categories.

Similarly, (**Zhou, and colleagues 2018**) performed a single-center prospective cohort study to evaluate the impact of BMI on the survival of a cohort of medical patients with sepsis at A tertiary care university hospital in China. A total of 178 patients with sepsis admitted to ICU were included. The 90-day mortality and in-hospital mortality were statistically different among the four groups. Differences in survival among the BMI groups, with the underweight patients showing a lower survival rate.

Additionally, (**Wacharasint and colleagues2013**) found that Obese patients had the lowest 28-day mortality followed by overweight patients while patients with BMI <25 kg/m2 had the highest mortality. While **(Arabi and colleagues 2013**) reported thatobese and very obese patients had lower hospital mortality compared to normal weight patients.

To sum up, (**Wang and colleagues 2017**) performed a systematic review and meta-analysis to evaluate the associations between overweight, obese, and morbidly obese with outcomes in septic patients. An online search the PubMed, Embase, Web of Science, Cochrane Library and ClinicalTrials. gov

databases was conducted and eight studies were included in this meta-analysis. Compared with patients with normal BMI, patients with BMI $\geq$ 25 kg/m^2 exhibited decreased mortality. In subgroup analysis, compared with normal-weight patients, overweight patients had lower mortality, whereas obese and morbidly obese patients did not exhibit significantly reduced mortality.

The mechanism of the correlation between BMI and mortality of sepsis is unclear. There are several potential reasons that could explain this. First, higher BMI resulted in more fat reserves, and patients could have a greater capacity to cope with the inflammatory response during sepsis and sepsis-associated acute lung injury. Furthermore, they may be able to tolerate extensive weight loss and dysfunction associated with critical illness(**Stapleton et al.**, **2010**).

Second, a higher BMI can lead to an increased level of lipoproteins. High-density lipoproteins may bind and inactivate lipopolysaccharide or other harmful bacterial products released during sepsis and modulate adhesion molecule expression, upregulate endothelial nitric oxide synthase and counteract oxidative stress(**Wu et al.**, **2004**).

Third, higher BMI can lead to increased adipose tissue deposition. Adipose tissue is increasingly being considered as a functional endocrine organ and associated with increased renin-angiotensin system activity. It appears to have protective hemodynamic effects during sepsis and may decrease the need for fluid or vasopressor support(**Taylor et al.**, **2018**).

Another explanation is that obese patients had a significantly lower inflammatory cytokine profile than those with a normal BMI. Why obese patients have an altered IL-6 inflammatory response is not known. However, the finding of decreased circulating IL-6 concentrations in obese patients with sepsis is consistent with the observation of improved survival outcome **Taylor et al.**, **2018**)..

Nevertheless, the currently published literature is inconsistent regarding the effect of BMI on sepsis outcomes. In contrary to our findings, (**Papadimitriou-Olivgeris and colleagues 2016**) conducteda retrospective analysis of data of all patients admitted to the ICU of a tertiary hospital during a 28-month period to assess the correlation between sepsis, obesity, and mortality of patients admitted to an ICU. Of 834 patients included, 163 (19.5%) were obese, while 25 (3.0%) were morbidly obese. The results showed that there is increased mortality among obese ICU patients, obese patients had statistically lower survival than normal weight subjects.

Similarly, **Gaulton, and colleagues**(**Gaulton et al.**, **2015**) assessed whether BMI extremes are associated with increased 28-day mortality and hospital length of stay in emergency department patients presenting with severe sepsis. A retrospective chart review at an urban, level I trauma center of adults admitted with severe sepsis was conducted and 1,191 severe sepsis patients were included. There was no difference in adjusted mortality for underweight patients compared to the normal weight comparator. The obese and morbidly obese experienced decreased mortality risk, vs. normal BMI; however, after adjustment for baseline characteristics, this was no longer significant. There was no significant difference in LOS across BMI groups.

The exact causes of such discrepancies between our findings and the abovementioned studies are unclear. However, it can be attributed to many methodological differences. Moreover, patients' characteristics were apparently different in which some studies included only sepsis patients and excluded severe sepsis. The notable difference in sample size may be another factor. This inconsistency may also be partly due to the inability to control for history of chronic diseases, and to inadequate adjustment for several other confounders such as cigarette smoking, alcohol consumption, physical activity, and socioeconomic status.

Study's Limitations

The present study is one of the few studies that highlight the important role of BMI in sepsis mortality. Our study calls for further trials that assess the usefulness of routine examination of weight in sepsis patients. However, we acknowledge that the present study has some limitations. The sample size of the included patients was relatively small and from a single center which may limit the possibility that the study's results can be generalized to the general population.

5. Conclusion

In conclusion, obesity appears to be associated with a lower rate of mortality among septic patients. Since low BMI was associated with increased mortality in septic patients, we suggest that all populations at risk based on low BMI undergo a full nutrition assessment with a validated method. Nevertheless, further trials that assess the usefulness of BMI as a predictor of mortality in at-risk patients are still needed.

Recommendations and Limitations

- Obesity is a potential predictive characteristics for mortality among septic patients admitted to ICU.
- Since low BMI was associated with increased mortality in septic patients, we suggest that all populations at risk based on low BMI undergo a full nutrition assessment with a validated method.

- Nevertheless, further trials that assess the usefulness of BMI as a predictor of mortality in at-risk patients are still needed.
- We acknowledge that the present study has some limitations. The sample size of the included patients was relatively small and from a single center which may limit the possibility that the study's results can be generalized to the general population.

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