

## An-Najah National University Faculty of Graduate Studies

## THE PREVALENCE OF SEPSIS AND SEPTIC SHOCK: TREATMENT OUTCOMES AMONG ICU PATIENTS AT A TERTIARY HOSPITAL IN PALESTINE

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### Dedication

This thesis work is dedicated to my parents, who have always loved me unconditionally and whose good examples have taught me to work hard for the things that I aspire to achieve.

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### Declaration

I, the undersigned, declare that I submitted the thesis entitled:

#### THE PREVALENCE OF SEPSIS AND SEPTIC SHOCK: TREATMENT OUTCOMES AMONG ICU PATIENTS AT A TERTIARY HOSPITAL IN PALESTINE

I declare that the work provided in this thesis, unless otherwise referenced, is the researcher's own work, and has not been submitted elsewhere for any other degree or qualification.

Student's Name:

Signature:

Date:

### **List of Contents**

| Dedication III  |
|---|
| Acknowledgements IV   |
| Declaration   |
| List of Contents  |
| List of Tables  |
| List of FiguresIX   |
| List of Appendices  |
| AbstractXI  |
| Chapter One: Introduction and Theoretical Background 1                  |
| 1.1 Introduction  |
| 1.2 Definitions and Pathophysiology                                     |
| 1.3 Sequential Organ Failure Assessment                                 |
| 1.4 Prevalence of Sepsis and Septic Shock                               |
| 1.5 Predictors of Sepsis and Septic Shock, and Patients Characteristics |
| 1.6 The Impact of Sepsis and Septic Shock on Patient Mortality          |
| 1.7 Predictors of Mortality among Patients with Sepsis and Septic Shock |
| 1.8 The Impacts of Sepsis and Septic Shock on Patient' Length of Stay   |
| 1.9 The Impacts of Sepsis and Septic Shock on Other Outcomes            |
| 1.10 Definitions of the Study Variables                                 |
| 1.11 Problem Statement  |
| 1.12 Study Purpose  |
| 1.13 Significance of the Study  |
| 1.14 Research Questions   |
| Chapter Two: Methods15  |
| 2.1 Design  |
| 2.2 Settings  |
| 2.3 Sample and Sampling 15  |
| 2.4 Sample Size   |
| 2.5 Inclusion and Exclusion Criteria                                    |
| 2.6 Instruments   |
| 2.7 Validity and Reliability of the Instruments                         |
| 2.8 Ethical Considerations  |
| 2.9 Data Collection   |
| 2.10 Data analysis  |

| Chapter Three: Results   | 19 |
|--|----|
| 3.1 Prevalence sepsis and septic shock among the study participants of ICU patients        | 19 |
| 3.2 Infection site among sepsis group  | 20 |
| 3.3 Infection sites among septic shock group   | 21 |
| 3.4 Culture samples (blood, urine, and sputum) and types of bacteria among intensive units |    |
| 3.5 SOFA scores: Comparison of the three Groups' ICU patients                              | 25 |
| 3.6 Three group patients' characteristics comparisons                                      | 27 |
| Chapter Four: Discussion and Conclusion  | 32 |
| 4.1 Discussion of the key findings   | 32 |
| 4.2 Limitations of the study   | 35 |
| 4.3 Conclusions  | 35 |
| 4.4 Recommendations  | 35 |
| List of Abbreviations  | 36 |
| References   | 37 |
| Appendices   | 49 |
| الملخص   | ب  |

### List of Tables

| Table 3.1: Prevalence percentage of patients who developed sepsis and SS among the   |
|--|
| study participants of ICU patients   |
| Table 3.2: Infection sites among sepsis group  |
| Table 3.3: Infection sites among septic shock group                                  |
| Table 3.4: Positive culture samples    22  |
| Table 3.5: Blood culture: type of bacteria causing infection among ICU patients23    |
| Table 3.6: Urine culture: type of bacteria causing infection among ICU patients24    |
| Table 3.7: Sputum culture: type of bacteria causing infection among ICU patients 25  |
| Table 3.8: SOFA scores: Comparison of the three groups    26                         |
| Table 3.9: Three group patients' characteristics comparisons                         |
| Table 3.10: Lactate level, BP, LOS, and CCI among the three groups (none, sepsis, &  |
| septic shock)  |
| Table F.1: Mortality among the three groups (none, sepsis, & septic shock)           |
| Table F.2: Binary logistic regression for mortality and characteristics         54   |
| Table F.3: Area under the curve of lactate, SOFA, and CCI in predicting mortality 54 |
| Table F.4: Binary logistic regression for sepsis and characteristics         54      |
| Table F.5: Area under the curve of lactate, SOFA, and CCI in predicting sepsis       |

## List of Figures

| Figure 3.1: Infection sites among sepsis group                               |            |
|--|------------|
| Figure 3.2: Infection sites among septic shock group                         |            |
| Figure 3.3: SOFA scores: Comparison of the three groups                      | 27         |
| Figure 3.4: Area under the curve of lactate, SOFA, and CCI Index in          | predicting |
| mortality  |            |
| Figure 3.5: Area under the curve of lactate, SOFA, and CCI in predicting sep | sis31      |

## List of Appendices

| Appendix A: Patient ID number in the study                    |           |
|---|-----------|
| Appendix B: Patient's Data Collection Sheet                   |           |
| Appendix C: IRB Approval Letter                               | 51        |
| Appendix D: Permission from Makassed Hospital Ethics (Medical | Research) |
| Committee   |           |
| Appendix E: Permission from Makassed Hospital administration  | 53        |
| Appendix F: Tables of Study                                   | 54        |

#### THE PREVALENCE OF SEPSIS AND SEPTIC SHOCK: TREATMENT OUTCOMES AMONG ICU PATIENTS AT A TERTIARY HOSPITAL IN PALESTINE

By Huda Salah Mohmmad Odeh Supervisor Dr. Jamal Qaddumi

#### ABSTRACT

**Background:** Sepsis is a common health condition among patients admitted to the intensive care unit. Little is known on the prevalence of sepsis and septic shock and their health outcomes in the Palestinian hospitals.

**Objectives:** This study was conducted to describe retrospectively within the last two years the prevalence rate, mortality, and length of stay of adult patients with sepsis and septic shock in adult intensive care unit at Makassed Hospital in Palestine.

**Methods:** A correlational descriptive design was used in the current study. The study was conducted at Makassed Hospital in Palestine which provide a wide range of healthcare services. The data collection tools included sociodemographic details, Sepsis-3 to screen for sepsis and septic shock, Sequential Organ Failure Assessment scores, and Charlson Comorbidity Index.

**Results:** A total of 1101 patients were included in this analysis. The prevalence of sepsis and septic shock among the intensive care unit patients was 13.6%. Sequential Organ Failure Assessment scores were significantly higher for patients with septic shock compared to those with sepsis and those without sepsis. The mortality rate among the intensive care unit patients was 12%. Binary logistic regression and areas under receiver operating curves discrimination showed that Sequential Organ Failure Assessment score, Charlson Comorbidity Index, and length of stay in the intensive care unit were significant predictors of mortality.

**Conclusions:** Findings of this study showed that sepsis and septic shock are common life-threatening health conditions among patients admitted to intensive care unit in Palestine. Mortality rates were significantly higher when intensive care unit patients develop sepsis and septic shock.

Keywords: Sepsis, Septic shock, Prevalence, Intensive care unit, Hospitals, Mortality

## Chapter One Introduction and Theoretical Background

This chapter provides an introduction and a theoretical background to sepsis and septic shock with their outcomes among ICU patients. This chapter provides conceptual and operational definitions of the study variables and a brief review of the relevant literature. This chapter also describes the problem statement, research questions, and objectives of the study.

#### **1.1 Introduction**

Sepsis is a common health condition. It is a systemic harmful reaction of the body to infection (Levy et al., 2010; Robson & Daniels, 2013). Sepsis is a clinical syndrome characterized by organ dysfunction caused by a dysregulated response to infection which can lead to biologic, physiologic, and biochemical disturbances (Neviere, Parsons, & Finlay, 2017). Septic Shock (SS) is a distributive or vasodilatory shock characterized by hypotension, poor perfusion, no response for fluid resuscitation, and the need for vasopressors to maintain normal range of blood pressure (BP), mean arterial pressure (MAP), and serum lactate (Neviere et al., 2017). The problem of sepsis is still growing despite the advancements in care and supportive therapy (Riedemann, Guo, & Ward, 2003). Sepsis incidence increased threefold in the last 2 decades (Tanriover, Guven, Sen, Unal, & Uzun, 2006). It was found that sepsis has an incidence rate of 750,000 cases annually in the USA (Angus, Pires Pereira, & Silva, 2006). Unfortunately, sepsis was responsible for more than one-third of in-hospital deaths in the USA (Neviere et al., 2017). It was also found that sepsis can double mortality rate if it went without timely managed treatment, leading to high costs in healthcare (Levy et al., 2010; Marshall, Dellinger, & Levy, 2010), and bad effect on the worldwide health economics, with annual cost of more than 14 billion dollars (Picard, O'Donoghue, Young-Kershaw, & Russell, 2006). Moreover, around 45% of all intensive care unit (ICU) bed days and one-third of all the hospital bed days were occupied by patients with sepsis (Padkin et al., 2003).

#### **1.2 Definitions and Pathophysiology**

Sepsis is a "life-threatening organ dysfunction caused by a dysregulated host response to infection" (Singer, Deutschman, Seymour, Shankar-Hari, Annane, Bauer, Bellomo, Bernard, Chiche, & Coopersmith, 2016). On a continuum of severity from bad to the worst, sepsis can range from the early phase that starts with infection and bacteremia to sepsis and SS, leading to multiple organ dysfunction syndrome (MODS) and death (Neviere et al., 2017). Severe sepsis was defined as a dysregulated inflammatory response to infection which is associated with organ dysfunction, hypoperfusion, and hypotension (Neviere et al., 2017; Robson & Daniels, 2013). Systemic Inflammatory Response Syndrome (SIRS) was defined as having two or more abnormalities in heart rate, body temperature, white blood cell count, or respiration.

Recently, the Society of Critical Care Medicine (SCCM), the European Society of Intensive Care Medicine (ESICM), and other experts have dropped the term of SIRS from sepsis diagnostic criteria, because SIRS is not always caused by infection such the case with autoimmune diseases and thromboembolism (Neviere et al., 2017).

SS is a vasodilatory or distributive shock (Neviere et al., 2017), which is characterized by hypotension, poor perfusion, no response for fluid resuscitation, and the need for vasopressors to maintain normal range of BP (Neviere et al., 2017). It is a circulatory, metabolic, and cellular abnormalities that can increase the risk of mortality more than that sepsis does alone (Singer, Deutschman, Seymour, Shankar-Hari, Annane, Bauer, Bellomo, Bernard, Chiche, & Coopersmith, 2016). When a patient has SS, vasopressors are required to maintain MAP higher than 65 mmHg and serum lactate more than two millimole/liter in case of euvolemia (Singer, Deutschman, Seymour, Shankar-Hari, Annane, Bauer, Bellomo, Bernard, Chiche, & Coopersmith, 2016).

#### **1.3 Sequential Organ Failure Assessment**

Sequential Organ Failure Assessment (SOFA) is used to assess the development of multisystem organ failure and to assess the effects of various treatments on organ dysfunction or failure (J-L Vincent et al., 1996). SOFA is well known to the community of critical care. It can be scored retrospectively, manually, or by using electronic health record systems. Unfortunately, clinical and laboratory tests are required to assess patients based on these criteria (Singer, Deutschman, Seymour, Shankar-Hari, Annane, Bauer, Bellomo, Bernard, Chiche, & Coopersmith, 2016). Also, SOFA criteria is used to evaluate the following physiologic functions: respiration, central nervous system, renal, coagulation, hepatic, and cardiovascular functions (Jean-Louis Vincent, Mira, & Antonelli, 2016; J-L Vincent et al., 1996). The higher SOFA scores indicate the greater rates of patients' morbidity and mortality (Raith et al., 2017).

Other studies confirmed that SOFA scores could predict the mortality of adult patients with sepsis (Baykara et al., 2018). For patients with SS, the SOFA score was considered as an independent risk factor for mortality (P<.001) (fr, 2004). Specifically, the SOFA score was associated with 28-day mortality; the hazard ratio was 1.24 (95% CI 1.21-1.27) (P<.001) (Quenot et al., 2013). Moreover, for the association of SOFA score with 28-day mortality among patients with severe sepsis and SS, OR 1.078 (95% CI 1.018–1.141) (P=.01) (Huang, Tsai, Tsai, Yu, & Ko, 2015). Moreover, the 28-days mortality rate of patients with sepsis who achieved SOFA score of 0-5, 6-9, 10-11, and >11 were: 20%, 43%, 100%, and 100%, respectively (Ozaydin, Guneysel, Saridogan, & Ozaydin, 2017).

In the UK, Szakmany et al. (2018) found that SOFA was the best predictive model for 30day mortality (Area Under the Receiver Operating Characteristics (AUROC) 0.950 (95% CI 0.93–0.97), (P<.001) (Szakmany et al., 2018). In Brazil, Silva et al. (2019) found that for patients with sepsis whose SOFA scores were less than or equal to "two", their 30-day mortality rate was 13.83% (Silva et al., 2019). For patients with SOFA score greater than "two", their 30-day mortality rate was 42.27%, with a significant statistical difference (P<.001). Another study indicated that patients with severe sepsis or SS who had high SOFA scores, had higher mortality rates than patients with lower scores, and SOFA scores of survivors and non-survivors were  $5.70\pm3.4$  and  $9.30\pm3.7$ , respectively (P <.005). However, the type of mortality was not mentioned in this study and the old definition of sepsis was used (Paary, Kalaiselvan, Renuka, & Arunkumar, 2016).

During ICU stay, mean SOFA score of patients with sepsis alone was  $7.0 \pm 3.2$ , and  $10.1 \pm 3.9$  for patients with severe sepsis (Sakr et al., 2018). In Japan, the mean SOFA score of patients with severe sepsis was  $6.8 \pm 3.4$  (Ogura et al., 2014).

Furthermore, among adults with severe sepsis admitted to eight ICUs in China, a significant difference was found in total SOFA scores between survivors and non-survivors; the score was  $8.5\pm3.7$  for survivors and  $11.1\pm3.9$  for non-survivors (P<.001).

However, this score was calculated on the first day of admission to ICU, and three- fourth of the patients were admitted to medical ICUs (Chen, Cheng, Chan, & Yu, 2014).

#### **1.4 Prevalence of Sepsis and Septic Shock**

Sepsis and SS are common illnesses. The percentage of adult patients with sepsis in ICUs was doubled between the years 2008 and 2015, 6.4% in 2008 and 13.4% in 2015 (Relative ratio (RR)=1.11; P <.001) (Badawi, Liu, Hassan, Amelung, & Swami, 2018). A study revealed that 37.3% of adult patients admitted to 22 ICUs in China were diagnosed with severe sepsis or SS (Zhou et al., 2014). Sepsis prevalence ranged between 10.5 and 30 per 100 admissions in ICUs of different developed countries (Artero, Nogueira, & Zaragoza, 2012). Prevalence rates of sepsis were 12.6% in ICUs of Germany (Group, 2016), 11% in ICUs of the Netherlands (van Gestel, Bakker, Veraart, & van Hout, 2004), 11% to 27% in ICUs of Taiwan and 19% in a medical ICU in Thailand (Khassawneh, Khader, & Abuqtaish, 2009).

During the Hajj season of 2004 in Makkah, Baharoon et al. (2009) conducted a prospective study to assess the incidence, causes, complications, and outcome of sepsis and SS among adult patients in two ICUs (N=165) (Baharoon, Al-Jahdali, Al Hashmi, Memish, & Ahmed, 2009). Data were collected over one and a half months. The findings revealed that sepsis and SS together were responsible for 25.4% of ICU admissions. However, the study was conducted in the Hajj season, which is the pilgrim season of Muslims that does not represent the usual conditions of everyday life. This might limit the external validity of this study.

Salvo et al. (1995) conducted a one-year prospective multicenter study in 99 ICUs in Italy to determine the incidence, prevalence, and outcomes of sepsis among adult patients (N=1101) (Salvo et al., 1995). Sepsis, severe sepsis, and SS were responsible for 4.5%, 2.1%, and 3% of ICU admissions, respectively. However, this study used an old definition of sepsis, severe sepsis, and SS that was based on SIRS criteria. In addition, consecutive sampling was used in this study, which may justify the low prevalence rate.

An observational study was conducted by Padkin et al. (2003) to investigate the numbers and outcomes of adult patients with severe sepsis admitted to 91 ICU in the UK (Padkin et al., 2003). The results showed that 15,362 (27.1%) patients out of 56,673 patients developed severe sepsis in the first 24 hours of admission. Moreover, a prospective

observational study was conducted to assess the prevalence and outcomes of adult patients in surgical ICUs of ten hospitals in China (N=3,665). The findings revealed a prevalence rate of 8.68% for severe sepsis (Cheng et al., 2017). Another prospective descriptive study was conducted over six years in an ICU in Macedonia by Grozdanovski et al. (2018), to determine the epidemiology of community-acquired sepsis (Grozdanovski et al., 2018). There was a total of 1348 admissions, out of them, 277 (20.5%) patients had sepsis and SS. Furthermore, Hantrakun et al. (2018) conducted a prospective observational study to describe clinical epidemiology and outcomes of sepsis and community-acquired infection in resource- limited ICUs of a tertiary hospital in Thailand (N= 28,752) (Hantrakun et al., 2018). The researchers used the most recent definition of sepsis that was recommended by Sepsis-3 International Consensus in 2016. Out of these patients, 74% had sepsis. However, this high rate could happen because the study included patients with medical illnesses only.

#### 1.5 Predictors of Sepsis and Septic Shock, and Patients Characteristics

Some factors that predicted sepsis among adult patients in ICUs were: being elderly (Wang et al., 2014), male gender (Martin, Mannino, Eaton, & Moss, 2003; Mayr, Yende, & Angus, 2014), being diagnosed with a medical illness (Salvo et al., 1995), history of severe sepsis, having a surgical condition, genitourinary infection, organ dysfunction (Shen, Lu, & Yang, 2010), and respiratory infection (Gray et al., 2013; Khassawneh et al., 2009; McNevin, McDowell, Fitzpatrick, O'Sullivan, & Wakai, 2018; Shen et al., 2010; van Gestel et al., 2004; Zhou et al., 2014), like pneumonia (Baharoon et al., 2009; Mayr et al., 2014). Additional predictors of sepsis among adult patients were: having a chronic respiratory illness (Baharoon et al., 2009), having culture test positive for gram-negative microorganisms (Artero et al., 2012; Baharoon et al., 2009; Blanco et al., 2008; Khwannimit & Bhurayanontachai, 2009; Zhou et al., 2014), black race (Mayr et al., 2014), high early warning score, Chronic Obstructive Pulmonary Disease (COPD), smoking, alcohol abuse (Szakmany et al., 2018), heart failure, cancer (Szakmany et al., 2018; Zhou et al., 2014), nosocomial infection (Group, 2016), septicemia, having a urinary catheter (Kim, Watase, Jablonowski, Gatewood, & Henning, 2017), being hospitalized in ICU, having diabetes, immunosuppression, history of previous hospitalization (Neviere et al., 2017), and bacteremia that was evident in half of the patient with sepsis (Bone et al., 1989). Additional factors that predicted worsening of severe sepsis or SS in emergency department (ED) were: diastolic BP <52 mmHg, serum albumin <3.5 milligrams/ deciliter and being immunocompromised (Zhou et al., 2014).

In ICUs, many adult patients with sepsis had positive microbiological cultures. It was found that 24% of patients with sepsis and severe sepsis had positive blood cultures (Chimese, Andrews, & Lakhi, 2012). The percentage of adult patients with sepsis who had positive blood cultures was 22.7% (Grozdanovski et al., 2018), 33% (Boussekey et al., 2010), and 40.9% (Ogura et al., 2014). A larger percentage was found by Sakr et al. (2018), who found that 69.6% of patients with sepsis had positive blood cultures; one-third of them had gram-positive bacteria, and two-third had gram-negative bacteria (Sakr et al., 2018). Candida was positive in 2.6% of blood cultures of patients with sepsis (Boussekey et al., 2010). Moreover, Baharoon et al. (2015) found that gram-negative microorganisms were the most common cause of severe sepsis and SS among adult patients admitted in ICUs of a tertiary hospital in Saudi Arabia (Baharoon et al., 2015). Another study indicated that the most common microorganisms that caused sepsis and SS were gram-positive bacteria, like staphylococci, followed by gram- negatives like Acinetobacter baumannii, Enterobacter, Escherichia coli, Klebsiella pneumoniae, and Candida (Vendemiato, von Nowakonski, de Lima Marson, & Levy, 2015). However, another study found that Staphylococcus aureus and Streptococcus pneumoniae were the most commonly isolated microorganisms from blood cultures of patients with sepsis or severe sepsis (Chimese et al., 2012).

#### 1.6 The Impact of Sepsis and Septic Shock on Patient Mortality

Sepsis and SS can increase the mortality rate of adult patients in ICUs. In some patients, sepsis can lead to death within hours if left without timely-fashioned treatment (Rebeaud, 2017). Unfortunately, for every hour that treatment of sepsis was delayed, the mortality rate caused by sepsis increased by 8% (Kumar et al., 2006). Sepsis alone was responsible for an annual death rate of six million people at the global level (Fleischmann et al., 2016), most commonly in middle and low-income countries (Organization, 2017). It was estimated that about 250,000 Americans die due to severe sepsis each year, and that one-third of all patients who died in hospitals were diagnosed with severe sepsis. Moreover, the mortality rate was ranging between 28% and 50% for patients with severe sepsis in North America (Perman, Goyal, & Gaieski, 2012), and between 18% and 55% in Taiwan (Shen et al., 2010). Also, crude mortality rates of patients with sepsis in France were 62.1% and 55.9% in the years 1993 and 2000, respectively (P<.001) (Annane, Aegerter, Jars-Guincestre, & Guidet, 2003). It was revealed that among 311 patients with sepsis admitted to 14 ICUs of 13 hospitals in Spain, 169 (54.3%) patients died in the hospitals, and 150

(48.2%) patients died in the ICUs, and that 28-day mortality rate was 47.9% (Blanco et al., 2008). Furthermore, 54.7% of patients with sepsis and SS died in one ICU during the Hajj season of 2004 in Makkah (Baharoon et al., 2009).

Sepsis can increase the in-hospital mortality of adult patients in ICUs. In one medical ICU in India, the overall in-hospital mortality rate was 33.6% among patients with sepsis (Santhosh Kumar Thulaseedharan, Jasen, Suresh Moothezhathu, & Mohammed Naseem Yakoob, 2017). Fortunately, the in-hospital mortality rate decreased over a study period of six years, and the percentage of in-hospital mortality was 17% at the final year of the study; this study was prospective and observational, which aimed to assess the clinical characteristics and prognosis of patients with severe sepsis and SS in an ICU in Spain (N= 1136) (Azkárate et al., 2016). It was found that the percentage of in-hospital mortality of adult patients in hospitals of the USA with severe sepsis and SS was 14.9% and 34.2%, respectively (Paoli, Reynolds, Sinha, Gitlin, & Crouser, 2018). Furthermore, it was reported that 85% of patients with SS in a medical ICU in India died inside the hospital (Santhosh Kumar Thulaseedharan et al., 2017).

#### 1.7 Predictors of Mortality among Patients with Sepsis and Septic Shock

Some variables predicted in-hospital mortality of patients with sepsis. The predictors of inhospital mortality among adult patients with sepsis were: having SS (Ogura et al., 2014; Santhosh Kumar Thulaseedharan et al., 2017; Silva et al., 2019; Ullah et al., 2016), having disseminated intravascular coagulation, the score of cardiovascular SOFA item (Ogura et al., 2014), age (Kotfis et al., 2019), having a neurologic disease (Wang et al., 2014), lactate level, coagulopathy (Silva et al., 2019), and having mechanical ventilation (Tanriover et al., 2006). Other researchers found that while the in-hospital mortality rate of patients with severe sepsis for age group over 65 years was 40.0%, it was 20.4% for the age group under 65 years, with a significant association between age and in-hospital mortality rate (P<.05) (Karlsson et al., 2007). It was indicated that the mortality rate was lower among patients with sepsis who were younger than 44 years old (Kaukonen, Bailey, Suzuki, Pilcher, & Bellomo, 2014). But, another study indicated that age was not significantly associated with in- hospital mortality of adult patients with severe sepsis in ICUs (N=254) (Chen et al., 2014).

#### 1.8 The Impacts of Sepsis and Septic Shock on Patient' Length of Stay

Sepsis and SS can increase patients' ICU length of stay (LOS) and hospital LOS. It was found that hospital LOS of patients with sepsis was 75% longer than for patients with no sepsis. A possible factor for this issue was that sepsis could lead to failure of body organs (Opal & Van Der Poll, 2015). While mean hospital LOS of severe sepsis survivors and non-survivors was 35 days and 15 days, respectively, mean ICU LOS of severe sepsis survivors and non-survivors was 12 days and 8 days, respectively (P<.01) (Blanco et al., 2008). A study was conducted in 47 ICU in the Netherlands revealed that mean ICU LOS of patients with sepsis, severe sepsis, and SS was 12.7 days (SD=1),13.3 days (SD=1.1), and 11.6 days (SD=1.5), respectively (van Gestel et al., 2004). In one tertiary hospital in Thailand, mean ICU LOS was three days and mean hospital LOS was 13 days (P<.001) among patients with severe sepsis and SS (Khwannimit & Bhurayanontachai, 2009). Moreover, mean ICU LOS and mean hospital LOS of patients with severe sepsis were 11 days and 24 days, respectively, in 133 ICUs in Germany (Group, 2016), 10.5 days (range=1-81), and 7.2 days for patients with SS in the USA (median=4±9.2) (Paoli et al., 2018). Baharoon et al. (2015) reported that the mean ICU LOS of patients with severe sepsis and SS was 17.19 days (SD=20.24) in wards and ICUs of a tertiary hospital in Saudi Arabia (Baharoon et al., 2015). However, the sample size was small (N=96).

Using a retrospective observational design, Paoli et al. (2018) analyzed data of patients who were admitted between January 2010 and September 2016 in academic and private hospitals in the USA (N=2,566,689) (Paoli et al., 2018). The results showed that mean hospital LOS of patients with sepsis without organ failure, severe sepsis, and SS was 7.7 days (median= $5\pm14.2$ ), ten days (median= $7\pm12.4$ ), and 12.6 days (median= $9\pm15.5$ ), respectively. However, this study relied on electronic coding, which might do not agree with the real clinical situation of patients. A recent study showed that the mean LOS of patients with severe sepsis was 30 days (range=14.2-45.7), and 22 days (range=11.2-36.5) for patients with SS (Baykara et al., 2018). However, the researchers did not specify the type of LOS. In general, sepsis can increase patients' hospital and ICULOS.

#### 1.9 The Impacts of Sepsis and Septic Shock on Other Outcomes

Sepsis can lead to further complications. Patients with sepsis had a greater risk of developing secondary infections later on during hospitalizations, such as pneumonia and bloodstream infections (van Vught et al., 2016), and recurrent hospitalization (Ogura et al.,

2014). It was found that the readmission rate within 30 days was 62% among patients who were hospitalized for sepsis (Fingar & Washington, 2016). In addition, it was reported that sepsis decreased patients' quality of life (Winters et al., 2010), and led to a bad effect on functional abilities and activities of daily living (Iwashyna, Cooke, Wunsch, & Kahn, 2012). However, early detection and management of sepsis can enhance patients' outcomes (Bateson & Patton, 2015; Rebeaud, 2017).

Sepsis had a negative effect on treatment costs. It was documented that sepsis was the most expensive reason for hospitalization, every day in the USA around 55.5 US million dollars are being spent in hospitals to treat patients with sepsis, in more details, the annual rate of growth in sepsis costs in hospitals is three times the rate of the overall hospital costs, with 24 US billion dollars were being spent on sepsis treatment every year in the USA (Stulberg & Haut, 2018). A literature review of 34 studies showed that the cost of treating sepsis and its consequences was higher than the cost of treating myocardial infarction and heart failure (Hajj, Blaine, Salavaci, & Jacoby, 2018).

In summary, sepsis and SS are common illnesses that adult patients admitted to ICUs can experience. Some studies reported a prevalence rate of sepsis ranging between 6.3% and 54.3% in different countries. It was also found that sepsis can increase mortality, morbidly, patients' LOS, and healthcare costs. Sepsis led to further complications, such as recurrent readmissions, functional disabilities, and poor quality of life. Fortunately, some studies indicated that SOFA criteria were useful in diagnosing patients with sepsis. Moreover, some factors have predicted mortality of patients with sepsis, like total SOFA score, having comorbidities, and other clinical characteristics of patients.

#### **1.10 Definitions of the Study Variables**

The operational and theoretical definitions of the study variables are explained as follows:

**Sepsis:** Conceptually, sepsis is a dysregulated inflammatory response to infection combined with life- threatening organ dysfunction, which can lead to biologic, physiologic and biochemical disturbances. In sepsis, hypoperfusion and hypotension may occur (Singer, Deutschman, Seymour, Shankar-Hari, Annane, Bauer, Bellomo, Bernard, Chiche, & Coopersmith, 2016).

Operationally, by using the criteria explained in appendix A and appendix B, patients were screened to and diagnosed with sepsis by the researcher. Having infection and a total SOFA score of two or more was considered as sepsis (Singer, Deutschman, Seymour, Shankar-Hari, Annane, Bauer, Bellomo, Bernard, Chiche, & Coopersmith, 2016). Note that the term "sepsis" was used generally to indicate "severe sepsis" wherever it appears in this research study.

**Severe sepsis:** Conceptually, severe sepsis was defined as "sepsis plus sepsis-induced organ dysfunction or tissue hypoperfusion" (Dellinger et al., 2013). The reader can notice that this term overlap with the term of sepsis.

Operationally, the term "severe sepsis" was not assessed or used in the current study design because it is redundant with the term sepsis (Neviere et al., 2017; Singer, Deutschman, Seymour, Shankar-Hari, Annane, Bauer, Bellomo, Bernard, Chiche, & Coopersmith, 2016). "Severe sepsis" term is no longer used as part of the definitions of sepsis phenomena. Based on the recent definitions, "sepsis" is equivalent to "severe sepsis". However, the term "severe sepsis" was used in the chapter of literature review only, because it was used by the previous studies.

**Septic shock:** Conceptually, septic shock (SS) is a distributive or vasodilatory shock characterized by hypotension, poor perfusion, no response for fluid resuscitation (Neviere et al., 2017), and the need for vasopressors to maintain MAP  $\geq$  65 mmHg despite resuscitation with an adequate volume of fluids (Neviere et al., 2017; Singer, Deutschman, Seymour, Shankar-Hari, Annane, Bauer, Bellomo, Bernard, Chiche, & Coopersmith, 2016).

Operationally, patients were screened to and diagnosed with SS by the researcher according to the SS screening checklist (see appendix A). The following criteria were used, which include having lactic acid  $\geq 2$  and hypotension characterized by need vasopressor to keep MAP  $\geq 65$  despite adequate fluid resuscitation, in the absence if other cause of hypotension (Neviere et al., 2017; Singer, Deutschman, Seymour, Shankar-Hari, Annane, Bauer, Bellomo, Bernard, Chiche, & Coopersmith, 2016).

**Organ dysfunction or failure:** Conceptually, it is "a dysfunction to such a degree that normal homeostasis cannot be maintained without external clinical intervention".

Operationally, organ dysfunction was measured using SOFA criteria. The higher SOFA score indicates higher severity of organ dysfunction or a higher number of organs with dysfunction (see Appendix B).

**Period prevalence:** Conceptually, period prevalence is "the prevalence measured over an interval of time. It is the proportion of persons with a particular disease or attribute at any time during the interval".

Operationally, the number of adult patients diagnosed with sepsis and SS and admitted between the last two years stating since 1st April 2019 to the 1st April 2021 retrospectively divided by the total number of patients admitted in the adult ICUs of Makassed Hospital at the same period. Prevalence was expressed as a number out of 100 (Percentage %). While every patient with sepsis represented one case, a patient with recurrent sepsis events was counted as one also.

**Mortality rate:** Conceptually, death rate occur over period of time (Tanriover et al., 2006).

Operationally, mortality rate was the number of deaths that occur from all causes at the end period of hospitalization.

**Hospital length of stay (LOS):** Conceptually, patients' hospital LOS is "average number of days those patients spend in hospital".

Operationally, patients' hospital LOS was measured by counting the total number of days a patient stayed in the hospital, including ICU LOS. It was rounded to nearest 0.5 day.

**ICU length of stay:** Conceptually, number of calendar days spent in ICU (Marik & Hedman, 2000).

Operationally, patient ICU LOS was measured by counting the total number of days a patient stayed in the ICU. It was rounded to nearest 0.5 day.

#### **1.11 Problem Statement**

Sepsis is a heterogeneous condition in which multiple severe symptoms may develop rapidly (Fabien, 2017). Sepsis affects 31 million patients worldwide annually (Fleischmann et al., 2016). Some studies showed that sepsis had an incidence rate of 285 cases per 100,000 hospital admissions in Taiwan (Shen et al., 2010), and 240 cases per 100,000 admissions to acute care hospitals in the USA (Martin et al., 2003). Another study showed that in the ICUs, severe sepsis occurs in 11% to 27% of the patients (Shen et al., 2010).

The prevalence of sepsis among ICU patients ranged from 6% to 30% depending on sepsis definition used (Martin et al., 2003; Jean-Louis Vincent et al., 2006) and the prevalence rate of SS was 13.7% among 10,941 adult patients admitted in 14 ICUs in France (Quenot et al., 2013). In Jordan, a retrospective study reviewed laboratory values, epidemiology, and clinical features of neonates admitted to one hospital between 2012 and 2015 (Yusef, Shalakhti, Awad, Algharaibeh, & Khasawneh, 2018). The study showed that 68 episodes of sepsis happened during that period, and the risk factors that might be predisposed neonates to sepsis were being a preterm neonate, having infection with multi-drug resistant organisms (Yusef et al., 2018), and having resistant gramnegative bacteria (Khassawneh et al., 2009). Another retrospective study done in Palestine about epidemiology of sepsis and septic shock among ICU patient at a tertiary hospital that admitted from January 1, 2017, and December 31, 2018. The study found that 174 episodes of sepsis and SS happened during that period, 54% have infected with multi-drug resistant bacteria with an average mortality rate of 39.7% (Rabee et al., 2020).

It was documented that nurses have a vital role in the early identification and treatment of sepsis (Burney et al., 2012; Kleinpell, Blot, Boulanger, Fulbrook, & Blackwood, 2019). They can improve patients' healthcare by assessing patients for sepsis and applying evidence-based protocols of sepsis treatment (Lopez-Bushnell, Demaray, & Jaco, 2014; Robson & Daniels, 2013). Unfortunately, it was shown that late diagnosis was the most reported obstacle for treating sepsis patients (Burney et al., 2012). For this reason, it is crucial that nurses screen patients for sepsis and SS and respond instantly to the signs and symptoms of sepsis and implement the necessary treatment. Indeed, sepsis is not easy to identify; the signs and symptoms are similar to those that belong to other diseases and can be confusing (Gaieski, Edwards, Kallan, & Carr, 2013). Moreover, sepsis is usually under-reported because it happens in the presence of other comorbidities.

#### **1.12 Study Purpose**

The purpose of this study was to describe retrospectively within the last two years the prevalence rate, mortality, and LOS of adult patients with sepsis/septic shock in adult ICU at Makassed Hospital in Palestine.

#### 1.13 Significance of the Study

Sepsis is a common illness. Different studies showed that sepsis prevalence rates among adult patients in ICUs ranged between 6.3% and 53% (Angus et al., 2006; Group, 2016; van Gestel et al., 2004). A study revealed that the percentage of admissions of patients with sepsis was doubled from 3.9% to 9.4% in three acute care hospitals in the USA during the period between 2010 and 2015 (P<.001) (Mayr et al., 2014).

Studying sepsis is a research priority. The World Health Organization (WHO) (2017) identified future sepsis research priorities. One of them was the need to understand the epidemiological burdens of sepsis using reliable data based on recently standardized definitions of sepsis and SS. The Surviving Sepsis Campaign (SSC), a global sepsis initiative, recommended six top research priorities for sepsis and SS, one of them was studying which information identifies organ dysfunction (Coopersmith et al., 2018). Validation of sepsis screening tools, including SOFA, was recommended by Lester and Hartjes (2018) (Lester, Hartjes, & Bennett, 2018). Using a Delphi survey, Sun et al. (2017) indicated that critical care is an essential priority for nursing research in the Eastern Mediterranean region, including Palestine (Sun et al., 2017).

As noted from the reviewed literature, sepsis and SS among adults in Palestine did not receive enough focus and research studies, and no similar study was conducted in the country. The current study sought to answer this gap in knowledge. No information was found about the prevalence of sepsis among ICUs patients in Palestine. There just previous study that was mentioned previously, which described epidemiology of sepsis and SS that conducted in medical ICU without comparing between patient with sepsis and SS and patient not sepsis and SS, no described about predictor for sepsis and

mortality moreover SS diagnose in this study dependent on BP reading alone without lactic acid reading.

The current study results will add significant information to the body of nursing and medical literature about sepsis prevalence and patients' outcomes. Furthermore, this study provided baseline information about sepsis and SS in Palestine. As expected, this study will broaden the horizons of the awareness of nursing educators, physicians, administrators, researchers, and clinicians regarding this crucial issue in Palestine. It is expected that the findings of this study will help nurses, physicians, and other healthcare providers in obtaining more information about this crucial issue in order to encourage focusing on improving screening of patients with sepsis and SS in Palestine.

#### **1.14 Research Questions**

- What is the prevalence rate of sepsis and SS within the last two years period among adult patients admitted to adult ICUs at Makassed Hospital?
- What is the mortality rate among adult patients with sepsis and SS admitted to adult ICUs at Makassed Hospital?
- What are the predictors of mortality among adult patients with sepsis and SS admitted to adult ICUs at Makassed Hospital?
- What is the difference in hospital and ICU length of stay between adult patients with sepsis and SS and adult patients without sepsis and SS admitted to adult ICUs at Makassed Hospital?

## Chapter Two Methods

Chapter two describes the methodology used in this study. This chapter provides a detailed description of the study design, settings, sample size and sampling method, inclusion and exclusion criteria, instruments, ethical considerations, data collection, and data analysis.

#### 2.1 Design

A correlational descriptive design was used in the current study. This design can help describe and observe aspects of a phenomenon as they occurred. Furthermore, this design was appropriate to investigate relevant research problems (Alberti et al., 2002; Baharoon et al., 2009). The researcher of the current study described sepsis and SS prevalence, patients' outcomes in adult ICU at Makassed Hospital in Palestine.

#### 2.2 Settings

The study was conducted at Makassed Hospital in Palestine which provide a wide range of healthcare services. The adult ICU setting had 10 ICU beds.

#### 2.3 Sample and Sampling

All patients who were admitted to adult ICU at Makassed Hospital with age  $\geq 18$  years was the target population. However, retrospective sampling was used of patients admitted into the adult ICU during the two years period retrospectively between the time period of April 2019 to 1<sup>st</sup> of April 2021 at Makassed Hospital.

All patients who were admitted to the ICU in the selected hospital during the study period were included. Data relevant to age, gender, BP, SOFA score, CCI score, LOS in Adult ICU, LOS in hospital, mortality status were collected by the researcher for all groups of patients with sepsis, with SS and patients without sepsis and SS. Data relevant to the type of microorganisms, site of infection, if patient was on mechanical ventilator or have urinary catheter or central venous line were collected for patients diagnosed with sepsis and SS.

#### 2.4 Sample Size

The sample size was calculated using G\*Power software version 3.1 (Faul, Erdfelder, Lang, & Buchner, 2007). For calculation of sample size, the P level was set at (.05), the power level was set at (.80), and Effect Size (ES) was set at (.2). This value of ES fell at the borderline between small and medium effect size. Based on the entered values, the calculated total sample size (N) was 150 patients with sepsis and SS.

#### 2.5 Inclusion and Exclusion Criteria

Patients with suspected or confirmed sepsis were usually admitted via ED to the ICU if their conditions were deteriorating (Daniels, Nutbeam, McNamara, & Galvin, 2011). All Patients admitted in the adult ICU between the time period of 1<sup>st</sup> April 2019 to the 1<sup>st</sup> April 2021 were included. Additional eligibility criterion patient age  $\geq$  18 years (Grozdanovski et al., 2018; Jacobson, Johansson, & Winsö, 2004). Patient admitted for less than 24 hour were excluded and those who were readmitted at the same hospital were also excluded (Grozdanovski et al., 2018).

#### 2.6 Instruments

The first part of the instrument was a flowchart for screening patients with sepsis and SS, which was adapted from the study of the International Taskforce (Sepsis-3) by Singer et al. (2016) (see Appendix A) (Singer, Deutschman, Seymour, Shankar-Hari, Annane, Bauer, Bellomo, Bernard, Chiche, & Coopersmith, 2016). This instrument included the SOFA tool that first used by Vincent et al. (1996) to describe the degree of failure of six different body systems (see Appendix B) (J-L Vincent et al., 1996).

The second part of the instrument developed by the researcher to collect patients' sociodemographic characteristics and clinical variables. This instrument sought baseline information like age, gender, site of infection, having a urinary catheter or central venous line, name of microorganisms in microbiology cultures, having mechanical ventilation or not, ICU LOS, hospital LOS, mortality status, and other variables (see Appendix C).

The third part of the instrument measured comorbidities using the Charlson Comorbidity Index (CCI) (Çıldır et al., 2013).

#### 2.7 Validity and Reliability of the Instruments

The instruments were previously validated and tested for reliability (Arts, de Keizer, Vroom, & de Jonge, 2005; Çıldır et al., 2013; de Groot, Beckerman, Lankhorst, & Bouter, 2003; Lambden, Laterre, Levy, & Francois, 2019; Singer, Deutschman, Seymour, Shankar-Hari, Annane, Bauer, Bellomo, Bernard, Chiche, & Coopersmith, 2016; Singer, Deutschman, Seymour, Shankar-Hari, Annane, Bauer, Bellomo, Bernard, Chiche, Coopersmith, et al., 2016; J-L Vincent et al., 1996). The content validity, construct validity, predictive validity, and ecologic validity of Sepsis-3 were previously established through and expert consensus process (Singer, Deutschman, Seymour, Shankar-Hari, Annane, Bauer, Bellomo, Bernard, Chiche, Coopersmith, et al., 2016). Similarly, the reliability and accuracy of SOFA scoring was previously established (Arts et al., 2005; Lambden et al., 2019). Using a gold standard, the total SOFA scores showed a mean absolute deviation of 0.82 and the inter-rater reliability was more than 80%. Similarly, the CCI was shown to be valid with good test-retest and inter-rater reliability (de Groot et al., 2003).

In this study, the used tools were reviewed by experts in the domain who judged that the tools were suitable for use and can generate relevant data.

#### 2.8 Ethical Considerations

Approval to conduct the study was obtained from the Institutional Review Board (IRB) of An-Najah National University. Permission from the hospital administration and Makassed Hospital Ethics (Medical Research) Committee was obtained.

#### **2.9 Data Collection**

The study was based on a retrospective analysis of electronic patients ICU records from the 1<sup>st</sup> April 2019 to the 1<sup>st</sup> April 2021 of patients admitted to adult ICU at Makassed Hospital. Informed consent was not required for this retrospective study.

The initial screening of patients for sepsis and SS was carried out collaboratively by the researcher. Data were only collected from the adult ICU. All patients who were admitted to the adult ICU were evaluated for diagnose of sepsis or SS or None sepsis and SS.

Surviving sepsis campaign in 2021 defined sepsis consistently with The Third International Consensus definition (Sepsis-3) (Evans et al., 2021).

Inclusion criteria were  $\geq 18$  years. All patients admitted to Adult ICU between 1<sup>st</sup> April 2019 to the 1<sup>st</sup> April 2021 except patients who stayed in the ICU less than 24 hour and those who were readmitted to the hospital were excluded to ensure that a single individual was not counted multiple times as an admission in the data. This was done to prevent correlated data that would violate our regression principles (Norman, Cooke, Ely, & Graves, 2017).

Data collection comprised demographic data (age, gender, comorbidities, laboratory data, BP, ICU LOS, Hospital LOS and mortality status) for all patient admitted to Adult ICU but the Data relevant to the type of microorganisms, site of infection, if patient was on mechanical ventilator or have urinary catheter or central venous line were collected only for patients diagnosed with sepsis and SS.

SOFA was calculated for all patients admitted to Adult ICU that ranged from (0-24) by use worst reading in the first 24 hour follow ICU admission (Huang et al., 2015; Riedemann et al., 2003; Schlapbach, Straney, Bellomo, MacLaren, & Pilcher, 2018).

#### 2.10 Data analysis

The researcher entered the data into the Statistical Package for the Social Sciences (SPSS). Data were analyzed using SPSS version 23 (IBM Corp, 2015). Descriptive statistics (mean, median, standard deviation, range, percentage, and frequency) were used to describe sample characteristics and clinical variables. Suitable statistics were used depending on the level of measurement of the variables and their level of skewness. Thirty-day mortality was described by a nominal level of measurement (alive/dead). Hospital and ICU LOS were described by a continuous level of measurement (number of days). A Chi-square test, an independent samples t-test were performed to test the difference in hospital and ICU LOS among the two groups of patients. In addition, a binary logistic regression test was used to assess predictors of 30-day mortality among patients with sepsis.

## Chapter Three Results

Chapter three provides detailed results of the data collection and analysis used in this thesis. In this thesis, prevalence of sepsis and septic shock among ICU patients was measured and evaluated. In this chapter, details of the variables of the patients that were collected and analyzed are provided. Additionally, this chapter provides prevalence rates of sepsis and SS among patients admitted to the ICU, description of the infection site among sepsis and SS patients, details of the microorganisms identified in blood cultures, urine cultures, sputum cultures, SOFA scores, mortality rates, and predictors of mortality.

#### Results

This thesis was created in order to measure and evaluate the prevalence of sepsis and septic shock among ICU patients. Furthermore, to assess the demographic and characteristics variables of patients who are exposed to sepsis and the septic shock among those patients admitted to the critical care units. And, to know the variables that predict the occurrence of sepsis and the septic shock among the participants from the critical care patients. Finally, to assess the ability of some predictive tools in predicting the occurrence of mortality, sepsis and the septic shock among the participants from the critical care patients.

# **3.1 Prevalence sepsis and septic shock among the study participants of ICU patients**

Table 3.1 shows that the prevalence percentage of patients who developed sepsis reached 13.6%, where the percentage of sepsis without developing into shock was only 7.8%, while the percentage of those patients with whom the sepsis developed into SS was 5.8% among the study participants of ICU patients.

#### Table 3.1

Prevalence percentage of patients who developed sepsis and SS among the study participants of ICU patients

| -      | Variable | Category | Frequency | %    |
|--------|----------|----------|-----------|------|
| -      |          | None     | 951       | 86.4 |
| Sepsis | Sepsis   | 86       | 7.8       |      |
|        | SS       | 64       | 5.8       |      |
|        | Total    | 1101     | 100.0     |      |

Note. SS: Septic shock

#### 3.2 Infection site among sepsis group

Concerning the site of infection among the critical care patients who developed sepsis, the results showed that the urinary system was the most (33.3%) susceptible site to infection among patients, then followed by the blood (25.8%) and then the respiratory system (23.7%), while soft tissue, central nervous system and the digestive system, were the least susceptible site to infection (2.5%, 1.5%, and 1% respectively). See Table 3. 2 and Figure 3.1.

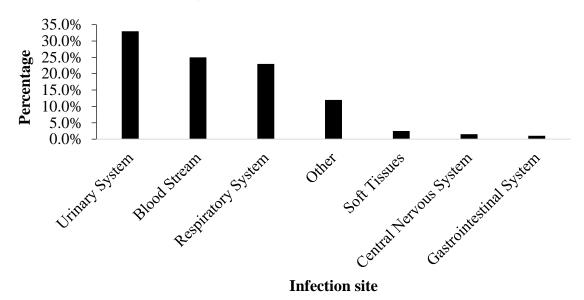
#### Table 3.2

Infection sites among sepsis group

| Infection site          | Frequency | %     |
|-------------------------|-----------|-------|
| Urinary System          | 66        | 33.3  |
| Blood Stream            | 51        | 25.8  |
| Respiratory System      | 47        | 23.7  |
| Other                   | 24        | 12.1  |
| Soft Tissues            | 5         | 2.5   |
| Central Nervous System  | 3         | 1.5   |
| Gastrointestinal System | 2         | 1.0   |
| Total                   | 198       | 100.0 |

#### Figure 3.1

Infection sites among sepsis group



#### 3.3 Infection sites among septic shock group

Concerning the site of infection among the critical care patients who developed septic shock, the results showed that the urinary system was the most (37.6%) susceptible site to infection among patients, then followed by the respiratory system (26.1%) and then the blood (19.7%), while the digestive system and soft tissue were the least susceptible site to infection (3.8% and 1.9% respectively). See Table 3.3 and Figure 3.2.

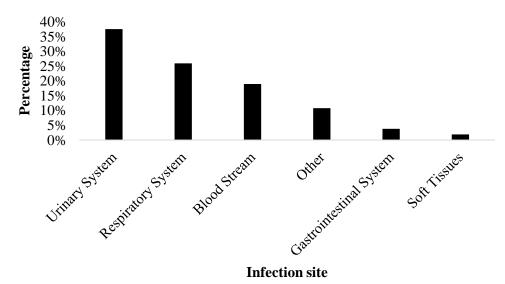
#### Table 3.3

| Infection site          | Frequency | %     |
|-------------------------|-----------|-------|
| Urinary System          | 59        | 37.6  |
| Respiratory System      | 41        | 26.1  |
| Blood Stream            | 31        | 19.7  |
| Other                   | 17        | 10.8  |
| Gastrointestinal System | 6         | 3.8   |
| Soft Tissues            | 3         | 1.9   |
| Total                   | 157       | 100.0 |

Infection sites among septic shock group

#### Figure 3.2

Infection sites among septic shock group



**3.4** Culture samples (blood, urine, and sputum) and types of bacteria among intensive care units patients

#### **3.4.1 Positive culture samples**

Regarding the percentages of positive culture samples among ICU, the results showed that the percentage of positive tests among the blood culture samples was 12.6%, while among the urine culture samples it was 12.5%, while among the sputum culture samples it was 10.6%. See Table 3.4.

#### Table 3.4

Positive culture samples

| Culture  | Result | Frequency | %    |
|----------|--------|-----------|------|
| Blood    | None   | 961       | 87.4 |
|          | Yes    | 139       | 12.6 |
| Urine    | None   | 962       | 87.5 |
|          | Yes    | 138       | 12.5 |
| Construm | None   | 983       | 89.4 |
| Sputum   | Yes    | 117       | 10.6 |

# **3.4.2** Type of bacteria causing infection among ICU patients in blood culture

As for the type of bacteria causing infection among ICU patients, the results showed that Coagulase negative staphylococcus was the most common bacteria present in blood culture samples, followed by Acinetobacter and Escherichia coli (3.8%, 0.8%, and 0.7% respectively). While VRE, Proteus spp., CRE was the least (0.1% for each). See Table 3.5.

#### Table 3.5

| Type of bacteria                  | Frequency | %    |
|-----------------------------------|-----------|------|
| None                              | 961       | 87.4 |
| Coagulase negative staphylococcus | 42        | 3.8  |
| Acinetobacter                     | 9         | 0.8  |
| Escherichia coli                  | 8         | 0.7  |
| Enterococcus spp.                 | 8         | 0.7  |
| Yeast                             | 6         | 0.5  |
| Pseudomonas spp.                  | 6         | 0.5  |
| Klebsiella                        | 6         | 0.5  |
| Staphylococcus aureus             | 4         | 0.4  |
| Diphtheroid spp.                  | 3         | 0.3  |
| MRSA                              | 3         | 0.3  |
| Streptococcus Other               | 3         | 0.3  |
| Streptococcus group D             | 2         | 0.2  |
| Enterobacter spp.                 | 2         | 0.2  |
| Morganella morganii               | 2         | 0.2  |
| Anaerobes                         | 2         | 0.2  |
| VRE                               | 1         | 0.1  |
| Proteus spp.                      | 1         | 0.1  |
| CRE                               | 1         | 0.1  |

Blood culture: type of bacteria causing infection among ICU patients

## 3.4.3 Type of bacteria causing infection among ICU patients in urine

#### culture

As for the type of bacteria causing infection among ICU patients, the results showed that Yeast was the most common bacteria present in urine culture samples, followed by Escherichia coli and Pseudomonas spp. (5.2%, 2.1%, and 1.3% respectively). While Coagulase negative staphylococcus, Proteus spp., and Citrobacter species was the least (0.1% for each). See Table 3.6.

#### Table 3.6

| Type of bacteria                  | Frequency | %    |
|-----------------------------------|-----------|------|
| None                              | 962       | 87.5 |
| Yeast                             | 57        | 5.2  |
| Escherichia coli                  | 23        | 2.1  |
| Pseudomonas spp.                  | 14        | 1.3  |
| Acinetobacter                     | 13        | 1.2  |
| Klebsiella                        | 9         | 0.8  |
| Enterobacter spp.                 | 4         | 0.4  |
| Enterococcus spp.                 | 4         | 0.4  |
| VRE                               | 3         | 0.3  |
| CRE                               | 3         | 0.3  |
| Streptococcus Other               | 2         | 0.2  |
| Diphtheroid spp.                  | 2         | 0.2  |
| Coagulase negative staphylococcus | 1         | 0.1  |
| Proteus spp.                      | 1         | 0.1  |
| Citrobacter species               | 1         | 0.1  |

Urine culture: type of bacteria causing infection among ICU patients

# **3.4.4** Type of bacteria causing infection among ICU patients in sputum culture

As for the type of bacteria causing infection among ICU patients, the results showed that Acinetobacter was the most common bacteria present in sputum culture samples, followed by Yeast and Pseudomonas spp. (3%, 2.7%, and 2.2% respectively). While Coagulase negative staphylococcus, Stenotrophomonas maltophilia, and Citrobacter species was the least (0.1% for each). See Table 3.7.

#### Table 3.7

| Type of bacteria                  | Frequency | %    |
|-----------------------------------|-----------|------|
| None                              | 983       | 89.4 |
| Acinetobacter                     | 33        | 3.0  |
| Yeast                             | 30        | 2.7  |
| Pseudomonas spp.                  | 24        | 2.2  |
| Klebsiella                        | 10        | 0.9  |
| Escherichia coli                  | 7         | 0.6  |
| Haemophilus influenzae            | 6         | 0.5  |
| MRSA                              | 5         | 0.5  |
| Enterobacter spp.                 | 4         | 0.4  |
| Staphylococcus aureus             | 4         | 0.4  |
| CRE                               | 2         | 0.2  |
| Streptococcus Other               | 2         | 0.2  |
| Proteus spp.                      | 1         | 0.1  |
| Coagulase negative staphylococcus | 1         | 0.1  |
| Stenotrophomonas maltophilia      | 1         | 0.1  |
| Citrobacter species               | 1         | 0.1  |

Sputum culture: type of bacteria causing infection among ICU patients

#### 3.5 SOFA scores: Comparison of the three Groups' ICU patients

As for the results of the SOFA test, the results reflect that the values of all system in the scale are generally higher among the patients who suffered from septic shock than the values of the other participants, and also, the participants who suffered from sepsis had higher values of all systems in the scale than the participants who did not have sepsis or septic shock, and these differences were significant. See Table 3.8 and Figure 3.3.

## Table 3.8

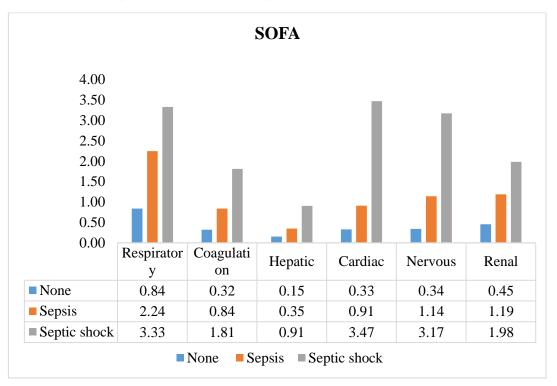
| SOFA scores: | Com | parison | of the | three | groups |
|--------------|-----|---------|--------|-------|--------|
|              |     |         |        |       |        |

|             |               |             |            | SEPSIS    |                 |         |  |
|-------------|---------------|-------------|------------|-----------|-----------------|---------|--|
| System      | SOFA<br>score | Total       | None       | Sepsis    | Septic<br>shock | P value |  |
|             | 0             | 431(39.3%)  | 430(45.4%) | 1(1.2%)   | 0(0.0%)         |         |  |
|             | 1             | 401(36.5%)  | 383(40.4%) | 17(19.8%) | 1(1.6%)         |         |  |
| Respiratory | 2             | 67(6.1%)    | 30(3.2%)   | 30(34.9%) | 7(10.9%)        | < 0.001 |  |
|             | 3             | 132(12.0%)  | 70(7.4%)   | 36(41.9)  | 26(40.6%)       |         |  |
|             | 4             | 67(6.1%)    | 35(3.7%)   | 2(2.3%)   | 30(46.9%)       |         |  |
|             | 0             | 795(72.3%)  | 737(77.7%) | 43(50.0%) | 15(23.4%)       |         |  |
|             | 1             | 171(15.6%)  | 138(14.5%) | 22(25.6%) | 11(17.2%)       |         |  |
| Coagulation | 2             | 87 (7.9%)   | 58(6.1%)   | 14(16.3%) | 15(23.4%)       | < 0.001 |  |
|             | 3             | 35(3.2%)    | 12(1.3%)   | 6(7.0%)   | 17(26.6%)       |         |  |
|             | 4             | 11(1.0%)    | 4(0.4%)    | 1(1.2%)   | 6(9.4%)         |         |  |
|             | 0             | 961(88.0%)  | 858(91.1%) | 66(76.7%) | 37 (57.8%)      |         |  |
|             | 1             | 55(5.0%)    | 38(4.0%)   | 11(12.8%) | 6 (9.4%)        |         |  |
| Hepatic     | 2             | 57(5.2%)    | 36(3.8%)   | 8(9.3%)   | 13(20.3%)       | < 0.001 |  |
|             | 3             | 13(1.2%)    | 6(0.6%)    | 1(1.2%)   | 6(9.4%)         |         |  |
|             | 4             | 6(0.5%)     | 4(0.4%)    | 0(0.0%)   | 2(3.1%)         |         |  |
|             | 0             | 828(75.3%)  | 817(86.1%) | 11(12.8%) | 0(0.0%)         |         |  |
|             | 1             | 128 (11.6%) | 55(5.8%)   | 73(84.9%) | 0(0.0%)         |         |  |
| Cardiac     | 2             | 3(0.3%)     | 1(0.1%)    | 1(1.2%)   | 1(1.6%)         | < 0.001 |  |
|             | 3             | 84(7.6%)    | 51(5.4%)   | 1(1.2%)   | 32(50.0%)       |         |  |
|             | 4             | 56(5.1%)    | 25(2.6%)   | 0(0.0%)   | 31(48.4%)       |         |  |
|             | 0             | 866(79.0%)  | 823(87.0%) | 42(48.8%) | 1(1.6%)         |         |  |
|             | 1             | 26(2.4%)    | 14(1.5%)   | 6(7.0%)   | 6(9.4%)         |         |  |
| Nervous     | 2             | 95(8.7%)    | 58(6.1%)   | 27(31.4%) | 10(15.6%)       | < 0.001 |  |
|             | 3             | 29(2.6%)    | 12(1.3%)   | 6(7.0%)   | 11(17.2%)       |         |  |
|             | 4             | 80(7.3%)    | 39(4.1%)   | 5(5.8%)   | 36(56.3%)       |         |  |
|             | 0             | 754(68.5%)  | 707(74.4%) | 34(39.5%) | 13(20.3%)       |         |  |
|             | 1             | 167(15.2%)  | 136(14.3%) | 24(27.9%) | 7(10.9%)        |         |  |
| Renal       | 2             | 91(8.3%)    | 54(5.7%)   | 14(16.3%) | 23(35.9%)       | < 0.001 |  |
|             | 3             | 42(3.8%)    | 26(2.7%)   | 6(7.0%)   | 10(15.6%)       |         |  |
|             | 4             | 46(4.2%)    | 27(2.8%)   | 8(9.3%)   | 11(17.2%)       |         |  |

SOFA: Sequential Organ Failure Assessment

#### Figure 3.3

SOFA scores: Comparison of the three groups



#### 3.6 Three group patients' characteristics comparisons

The proportion of males and females was almost equal (51.3% and 48.7% respectively) among the ICU patients participating in the study, but the proportion of males was slightly higher among the patients who were develop sepsis (60.5%) or septic shock (50.8%) comparing with females (39.5% and 49.2%), but this difference was not statistically significant.

The results showed that all patients in the sepsis and SS groups had urine folly's catheter, while the proportion of patients with CV-Line and on mechanical ventilator was statistically significantly higher in the SS patients group (98.4% and 89.1% respectively) compared with the proportion of patients in sepsis group (43% and 43% respectively). ANOVA and Post hoc comparisons revealed that patients in non-sepsis group was statistically significant younger (53.8 years) than other patients in both sepsis (59.3 years) and septic shock (64.3 years) patients group. See Table 3.9.

## Table 3.9

Three group patients' characteristics comparisons

|           |        |             |             | SEPSIS     |              |                      |
|-----------|--------|-------------|-------------|------------|--------------|----------------------|
|           |        | Total       | None        | Sepsis     | Septic shock | -                    |
| Age       | M (SD) | 54.8(19.6)  | 53.8(19.6)  | 59.3(19.5) | 64.3(17.5)   | F= 10.82 (<.001)     |
|           |        | n(%)        | n(%)        | n(%)       | n(%)         | $X^2$ (p value)      |
| Gender    | Male   | 559(51.3%)  | 475(50.5%)  | 52(60.5%)  | 32(50.8%)    | 1 22 (0 24)          |
|           | Female | 531(48.7%)  | 466(49.5%)  | 34(39.5%)  | 31(49.2%)    | 1.38 (0.24) ∞        |
| E = 112 = | None   | 0(0%)       | 0(0.0%)     | 0(0.0%)    | 0(0.0%)      | NT A                 |
| Folly's   | Yes    | 1101(100%)  | 951(100.0%) | 86(100.0%) | 64(100.0%)   | NA                   |
| CVP Line  | None   | 1001(90.9%) | NA          | 49(57.0%)  | 1(1.6%)      | 50.7(0.001)          |
| CVP Line  | Yes    | 100(9.1%)   | NA          | 37(43.0%)  | 63(98.4%)    | <b>50.7(0.001)</b> ∞ |
| NAX7      | None   | 1007(91.5%) | 846(88.9%)  | 49(57.0%)  | 7(10.9%)     | 22.2(0.001)          |
| MV        | Yes    | 94(8.5%)    | 105(11.0%)  | 37(43.0%)  | 57(89.1%)    | 33.2(0.001) ∞        |

 $\infty X^2$  Conducted between sepsis and septic shock groups

It is clear through the ANOVA statistical analysis that the mean of the variables such as lactate, systolic blood pressure, diastolic blood pressure, LOS ICU, duration of hospital stay, and the CCI were statistically significant different (p values < 0.001) among the three groups (none, sepsis, and septic shock). Therefore, through the post hoc comparisons, it was found that all three groups were different regarding lactate, systolic and diastolic blood pressure and the CCI, while statistically significant differences in means of the duration in hospital and in intensive care unit were related to the group of patients who did not develop sepsis or septic shock. See Table 3.10.

#### Table 3.10

| Variable     | Group        | Ν    | Mean   | SD    | F     | P value |
|--------------|--------------|------|--------|-------|-------|---------|
|              | None         | 141  | 3.1    | 3.5   |       |         |
| Lactate      | Sepsis       | 86   | 1.16   | 0.44  | 27.14 | <.001   |
|              | Septic shock | 63   | 4.49   | 2.84  |       |         |
|              | Total        | 290  | 2.83   | 3.03  |       |         |
|              | None         | 950  | 117.01 | 16.81 |       |         |
| SBP          | Sepsis       | 71   | 86.51  | 8.18  | 270.9 | <.001   |
|              | Septic shock | 55   | 76.16  | 8.35  |       |         |
|              | Total        | 1076 | 112.91 | 19.68 |       |         |
|              | None         | 950  | 66.7   | 11.72 |       |         |
| DBP          | Sepsis       | 71   | 47.85  | 6.58  | 210.1 | <.001   |
|              | Septic shock | 55   | 41.53  | 6.88  |       |         |
|              | Total        | 1076 | 64.17  | 13.26 |       |         |
|              | None         | 946  | 2.22   | 3.35  |       |         |
| LOS ICU      | Sepsis       | 85   | 21.45  | 34.43 | 203.2 | <.001   |
|              | Septic shock | 63   | 24.78  | 24.52 |       |         |
|              | Total        | 1094 | 5.01   | 13.61 |       |         |
|              | None         | 948  | 8.85   | 7.38  |       |         |
| LOS Hospital | Sepsis       | 85   | 28.48  | 34.98 | 128.7 | <.001   |
|              | Septic shock | 63   | 26.51  | 24.83 |       |         |
|              | Total        | 1096 | 11.38  | 14.74 |       |         |
|              | None         | 950  | 1.83   | 1.77  |       |         |
| CCI          | Sepsis       | 86   | 3.64   | 1.75  | 93.14 | <.001   |
|              | Septic shock | 63   | 4.4    | 2.34  |       |         |
|              | Total        | 1099 | 2.12   | 1.95  |       |         |

Lactate level, BP, LOS, and CCI among the three groups (none, sepsis, & septic shock)

LOS: length of stay

As for the death rate, it was found that 12% of the intensive care patients died, and through cross tabulation analysis, it was found that nearly 70% of the group of patients with whom the Septic Shock developed died, while the deaths were about 23% of the

patients who developed Sepsis. On the contrary, the death rate was nearly 7% among patients who did not develop sepsis or septic shock. And these differences in death proportions among the three groups were statistically significant (X2= 280.2, p value <0.001). See Table 3.11 in Appendix F.

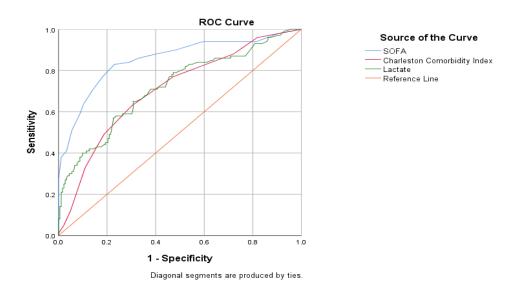
Logistic regression was used to analyze the relationship between demographic and characteristics of patients and mortality. Binary logistic regression revealed that SOFA (p < 0.001, exp (B) = 1.3), CCI (p = 0.044, exp (B) = 1.22), duration stay in ICU (p = 0.021, exp (B) = 1.03), was statistically significant (p values < 0.05) with mortality while the other variables were not statistically significant (p values > 0.05). See Table 3.12 in Appendix F.

The areas under receiver operating curves discrimination (area under the ROC curve; 95% CI): lactate (.719; CI= .655 - .783), SOFA (.853; CI= .803 - .903), CCI (.705; CI = .641 - .768) in prediction of mortality.

SOFA showed the best highest discriminative power, followed by lactate. CCI showed lower discriminative power in prediction of hospital mortality outcomes comparing with SOFA as seen in Figure 3.4 and Table 3.13 in Appendix F.

#### Figure 3.4

Area under the curve of lactate, SOFA, and CCI Index in predicting mortality



Logistic regression was used to analyze the relationship between demographic and characteristics of patients and sepsis. Binary logistic regression revealed that SOFA (p < 0.001, exp (B) = 1.28), CCI (p = 0.050, exp (B) = 1.21), duration stay in ICU

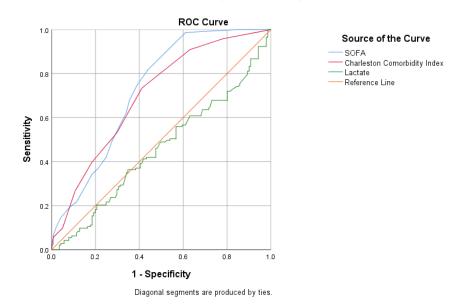
(p =0.027, exp (B) = 1.03), was statistically significant (p values < 0.05) with sepsis and septic shock while the other variables were not statistically significant (p values > 0.05). See Table 3.14 in Appendix F.

The areas under receiver operating curves discrimination (area under the ROC curve; 95% CI): lactate (.456; CI= .3895 - .523), SOFA (.725; CI= .666 - .785), CCI (.699; CI = .639 - .760) in prediction of mortality.

SOFA showed the best highest discriminative power, followed by CCI. Lactate showed lower discriminative power in prediction of hospital sepsis and septic shock outcomes comparing with SOFA as seen in Figure 3.5 and Table 3.15 in Appendix F.

#### Figure 3.5

Area under the curve of lactate, SOFA, and CCI in predicting sepsis



## **Chapter Four**

## **Discussion and Conclusions**

Chapter four discusses the results obtained in this thesis, interprets the key findings in this thesis, describes the limitations of the study, provides a conclusion, and finally provides recommendations.

#### 4.1 Discussion of the key findings

In this study, the prevalence of sepsis and SS was 13.6% among the patients admitted to the ICU. Findings of this study were consistent with those reported in the USA (Badawi et al., 2018), Germany (Group, 2016), the Netherlands (van Gestel et al., 2004), Taiwan, and Thailand (Khassawneh et al., 2009). On the other hand, the prevalence of sepsis and SS reported in this study was lower than those reported in China and Makkah (Baharoon et al., 2009; Zhou et al., 2014). Differences in the prevalence rates could be attributed to the fact that Baharoon et al's study was conducted during the Hajj season. During this season, millions of Muslims from all over the world are gathered in Makkah for a short period of time. It is also important to note that a considerable percentage of the pilgrims are elderly. These should have limited the external validity of their findings to normal settings.

Regarding the sites of infection, the urinary system had the most infections in both groups: sepsis and SS. Similarly, blood and respiratory infections were also among the most common sites of infections in both groups. This was consistent with the percentage of urine, blood, and sputum positive cultures in this study. In Zhou et al's study, pneumonia, urinary tract infections, bloodstream infections, and soft tissue infection were common among patients who developed sepsis and SS in the ICU (Zhou et al., 2014). In this study, 12.6% of the blood cultures were positive. This percentage was lower than those reported in previous studies in which bacterial isolates were identified in 22.7% to 69.6% of the samples (Baharoon et al., 2015; Boussekey et al., 2010; Chimese et al., 2012; Grozdanovski et al., 2018; Ogura et al., 2014; Sakr et al., 2018; Vendemiato et al., 2015). These discrepancies could be explained by differences in the methods used and populations of the patients included. When the causative agent was identified, findings of this study showed that 3.8% of the blood cultures were positive for Coagulase negative staphylococcus. Additionally, more than 0.5% of the

blood samples were positive for Acinetobacter, Escherichia coli, Enterococcus spp., Yeast, Pseudomonas spp., and Klebsiella. In urine samples, Yeast, Escherichia coli, and Pseudomonas spp. were the most prevalent species. In sputum samples, Acinetobacter, Yeast, and Pseudomonas spp. were the most prevalent species. These species were previously identified in isolates from Saudi Arabia, Mainland China, and elsewhere (Baharoon et al., 2009; Chimese et al., 2012; Vendemiato et al., 2015; Zhou et al., 2014).

The SOFA scores obtained in this study were significantly higher for all 6 organ systems (respiratory, blood, hepatic, cardiac, nervous, and renal) when patients who had not developed sepsis or SS, those who developed sepsis, and those who developed SS in the ICU. These graded elevations in the SOFA scores reflected the multi-system deteriorations that were consistent with the severity of the condition developed (SS > sepsis > no sepsis or SS). Findings of this study were consistent with those previously reported among ICU patients who developed sepsis and SS (Chen et al., 2014; Ogura et al., 2014; Sakr et al., 2018). Findings of this study might also add to the suitability and validity of using SOFA scores in assessing/monitoring ICU patients in Palestine.

In this study, the proportions of male and female patients were not statistically different across the three groups. However, male patients were more likely to develop sepsis. Moreover, patients in the SS group were more likely to receive urine folly's catheter, CV-Line, and mechanical ventilation compared to the patients in the other groups. On the other hand, patients who did not develop sepsis or SS were significantly younger than those in the sepsis and SS groups. These findings were consistent with the SOFA scores obtained in this study and reflected multi-organ failures (fr, 2004; Ozaydin et al., 2017; Quenot et al., 2013; Raith et al., 2017; Szakmany et al., 2018). Additionally, findings of this study were consistent with those previously reported in which being elderly and of male gender were predictors of developing sepsis (Martin et al., 2003; Mayr et al., 2014; Wang et al., 2014). Moreover, the patients who had multi-organ failures as a result of either having comorbidities, being infected with gram-negative bacteria, or developing severer health condition in the ICU were more likely to experience multi-organ system failures, receive urine catheter, and mechanical ventilation compared to patients who did not have commodities, were not infected with gram-negative bacteria, or did not developing severer health condition in the ICU (Baharoon et al., 2009; Gray et al., 2013; Khassawneh et al., 2009; Kim et al., 2017; Mayr et al., 2014; McNevin et al., 2018; Salvo et al., 1995; Shen et al., 2010; van Gestel et al., 2004; Zhou et al., 2014).

Findings of this study showed that lactate, LOS ICU, duration of hospital stay, and CCI were significantly higher for patients who developed SS compared to those who developed sepsis and those who did not develop neither sepsis nor SS. On the other hand, systolic and diastolic BP were significantly higher for patients who did not develop neither sepsis nor SS compared to those who developed sepsis and those who developed SS. These findings were consistent with the SOFA scores and developing severe health condition in the ICU as reported in this study. Additionally, findings of this study were consistent with those reported in previous studies in which developing SS was associated with multi-organ system failures, LOS ICU, and length of hospital stay (Baharoon et al., 2015; Blanco et al., 2008; Khwannimit & Bhurayanontachai, 2009; Opal & Van Der Poll, 2015; Paoli et al., 2018; van Gestel et al., 2004).

The mortality rates in this study were significantly higher among patients who developed SS in the ICU compared to those who developed sepsis and those who did not develop sepsis or SS. Findings of this study were consistent with those reported in previous studies in which mortality rates were between 18% to 62.1% among patients with SS (Annane et al., 2003; Azkárate et al., 2016; Baharoon et al., 2009; Blanco et al., 2008; Kumar et al., 2006; Perman et al., 2012; Rebeaud, 2017; Shen et al., 2010). Discrepancies in these rates could be attributed to differences in definitions of sepsis and SS, methods, and populations of the patients included. In this study, binary logistic regression and areas under receiver operating curves discrimination showed that SOFA score, CCI, and LOS ICU were significant predictors of mortality. Of these variables, SOFA scores were the most powerful discriminatory criterion that could be used to predict mortality. Findings of this study substantiates the power and usefulness of SOFA as an important tool in assessing and monitoring ICU patients (Ozaydin et al., 2017; Quenot et al., 2013; Raith et al., 2017; Silva et al., 2019; Szakmany et al., 2018).

#### 4.2 Limitations of the study

This study has a number of limitations that should be considered when interpreting the findings. The limitations of this study were:

- First, a retrospective design was used in this study. Compared to prospective designs, retrospective designs are less reliable and more prone to bias.
- Second, this was a single center study. In this study, the patients were included from one center. However, inclusion of patients from more than one center should have produced more reliable and representative data and should have improved the external validity of the findings.
- Third, the patients included over a relatively short period of time. Although the time period was two years, extending the time period could have allowed inclusion of a larger number of patients. Some previous studies have included a larger sample size which should have yielded more reliable results.

## **4.3 Conclusions**

In conclusion, findings of this study showed that sepsis and SS are common lifethreatening health conditions among patients admitted to ICU in Palestine. Development of such health conditions were shown to be associated with significant morbidity and mortality. Mortality rates were significantly higher when ICU patients develop sepsis and SS. Findings of this study showed that mortality can be predicted by SOFA score, CCI, and LOS ICU. Among these variables, SOFA is the most powerful discriminatory criterion.

#### 4.4 Recommendations

The key recommendations that can be derived from this study are:

- Decision makers in the Palestinian healthcare authorities should plan to address the possibility of development of sepsis and SS among ICU patients.
- Healthcare professionals who care for ICU patients might consider using SOFA score, CCI, and LOS ICU are predictors of mortality among the patients.
- More studies are still needed to design measures to decrease incidence of sepsis and SS among patients admitted to ICU in Palestine.

## List of Abbreviations

| Abbreviation | Meaning   |
|--------------|---|
| AUROC        | Area Under the Receiver Operating Characteristics |
| BP           | Blood pressure                                    |
| CCI          | Charlson Comorbidity Index                        |
| COPD         | Chronic Obstructive Pulmonary Disease             |
| ED           | Emergency department                              |
| ES           | Effect Size                                       |
| ESICM        | European Society of Intensive Care Medicine       |
| ICU          | Intensive care unit                               |
| IRB          | Institutional Review Board                        |
| LOS          | Length of stay                                    |
| MAP          | Mean arterial pressure                            |
| MODS         | Multiple organ dysfunction syndrome               |
| RR           | Relative ratio                                    |
| SCCM         | Society of Critical Care Medicine                 |
| SIRS         | Systemic Inflammatory Response Syndrome           |
| SOFA         | Sequential Organ Failure Assessment               |
| SPSS         | Statistical Package for the Social Sciences       |
| SS           | Septic shock                                      |
| SSC          | Surviving Sepsis Campaign                         |
| WHO          | World Health Organization                         |

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## Appendices

## Appendix A

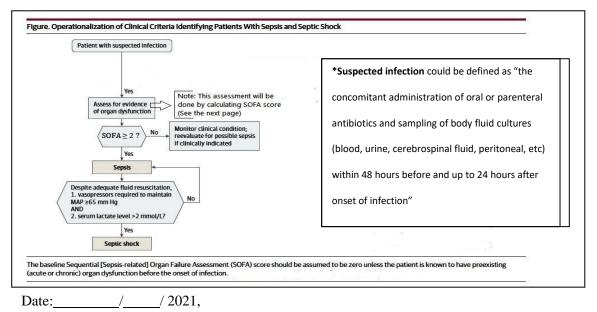
## Patient ID number in the study

Sepsis/Septic Shock Screening Flowchart (to be filled by researcher ) Patient's Medical Record Number:

Name and signature of the staff nurse:

Patient ID number in the study:

Site of the suspected infection (Body organ):



Time: \_\_\_\_\_(24 hr. clock) (date and time of sepsis or septic shock diagnosis).

Note: Please circle the applicable words (Yes/No) on the flowchart.

#### Sequential Organ Failure Assessment (SOFA) Tool (to be filled by the researcher)

Please circle the applicable parameters only and use the worst parameters measured during the prior 24 hours

|   | Score                    |                             |  |  |  |  |  |  |  |  |
|---|--------------------------|-----------------------------|--|--|--|--|--|--|--|--|
| System  | 0                        | 1                           | 2  | 3  | 4  |  |  |  |  |  |
| Respiration   |                          |                             |  |  |  |  |  |  |  |  |
| Pao <sub>2</sub> /Fio <sub>2</sub> , mm Hg<br>(kPa) | ≥400 (53.3)              | <400 (53.3)                 | <300 (40)  | <200 (26.7) with<br>respiratory support  | <100 (13.3) with<br>respiratory support                                    |  |  |  |  |  |
| Coagulation   |                          |                             |  |  |  |  |  |  |  |  |
| Platelets, ×10 <sup>3</sup> /µL                     | ≥150                     | <150                        | <100   | <50  | <20  |  |  |  |  |  |
| Liver   |                          |                             |  |  |  |  |  |  |  |  |
| Bilirubin, mg/dL<br>(µmol/L)                        | <1.2 (20)                | 1.2-1.9 (20-32)             | 2.0-5.9 (33-101)                                     | 6.0-11.9 (102-204)   | >12.0 (204)  |  |  |  |  |  |
| Cardiovascular                                      | MAP ≥70 mm Hg            | MAP <70 mm Hg               | Dopamine <5 or<br>dobutamine (any dose) <sup>b</sup> | Dopamine 5.1-15<br>or epinephrine $\leq 0.1$<br>or norepinephrine $\leq 0.1^{b}$ | Dopamine >15 or<br>epinephrine >0.1<br>or norepinephrine >0.1 <sup>b</sup> |  |  |  |  |  |
| Central nervous system                              |                          |                             |  |  |  |  |  |  |  |  |
| Glasgow Coma Scale<br>score <sup>c</sup>            | 15                       | 13-14                       | 10-12  | 6-9  | <6   |  |  |  |  |  |
| Renal   |                          |                             |  |  |  |  |  |  |  |  |
| Creatinine, mg/dL<br>(µmol/L)                       | <1.2 (110)               | 1.2-1.9 (110-170)           | 2.0-3.4 (171-299)                                    | 3.5-4.9 (300-440)  | >5.0 (440)   |  |  |  |  |  |
| Urine output, mL/d                                  |                          |                             |  | <500   | <200   |  |  |  |  |  |
| bbreviations: Fio <sub>2</sub> , fracti             | on of inspired oxygen; M | AP, mean arterial pressure; | <sup>b</sup> Catecholamine doses a                   | re given as µg/kg/min for at   | least 1 hour.  |  |  |  |  |  |
| Pao <sub>2</sub> , partial pressure of o            | xygen.                   |                             | <sup>c</sup> Glasgow Coma Scale so                   | ores range from 3-15; highe  | r score indicates better   |  |  |  |  |  |

## Appendix B

## **Patient's Data Collection Sheet**

Medical Record Number Age (in years) Gender Male Female Site of infection (Body organ) Blood Pressure (mmHg) Having a urinary catheter at the time of sepsis or Yes No septic shock diagnosis Having a central venous catheter at the time of Yes No sepsis or septic shock diagnosis Having mechanical ventilation at the time of sepsis Yes No or septic shock diagnosis Result of blood culture Positive Negative Not done Result urine culture Positive Negative Not done Result of sputum culture Positive Not done Negative Result of other culture, please specify it: Positive Negative Not done ..... Type of the microorganism in the culture (if Blood Urine Other Sputum applicable) Total Sequential Organ Failure Assessment (SOFA) Score Length of stay in ICU (number of days) Length of stay in the hospital (number of days) Mortality Status Alive Dead Charlson Comorbidity Index\* Points Disease Myocardial Infarction 1 Congestive Heart Failure 1 Peripheral Vascular disease 1 Cerebrovascular disease Dementia 1 COPD 1 Connective Tissue disease Peptic Ulcer disease 1 **Diabetes Mellitus** 1 point if uncomplicated 2 points if end-organ damage Moderate to severe CKD 2 Hemiplegia 2 Leukemia 2 Malignant Lymphoma 2 Solid Tumor 2 points 6 points if metastatic 1 point if mild Liver disease 3 points if moderate to severe AIDS 6 points Total Score

## Appendix C

## **IRB** approval

An-Najah National University Faculty of medicine Sciences Health Institutional Review Board



جلمعة النجاح الوطنية كلية الطب وعلوم الصحة لجنة اخلاقيات البحث العلمي

Ref: Mas. May 2021/12

#### **IRB** Approval Letter

Study Title:

The Prevalence of sepsis and septic shock: Treatment Outcomes among ICU patients at a tertiary hospital in Palestine

Submitted: Huda Salah Odeh

Supervisor: Jamal Qaddumi

Date Approved: 16<sup>th</sup> May 2021

Your Study "The Prevalence of sepsis and septic shock: Treatment Outcomes among ICU patients ata tertiary hospital in Palestine." viewed by An-Najah National University IRB committee and was approved on 16<sup>th</sup> May 2021.

Hasan Fitian, MD

IRB Committee Chairman An-Najah National University

\_\_\_\_ نابلس - ص.ب 7 أو 707 || هاتف 2342902/4/7/8/14 (09) (090) || فاكسيل 2342910 (09) (090)

Nablus - P.O Box :7 or 707 | Tel (970) (09) 2342902/4/7/8/14 | Faximile (970) (09) 2342910 | E-mail : hgs@najah.edu

# Appendix D

## Permission from Makassed Hospital administration

| 3 Jan 2000 03:05 HF                                | P Fax page 1   |
|--|--|
| Ø  | مستشفى جمعية المقاصد الخيرية الاسلامية – القدس<br>KASSED ISLAMIC CHARITABLE HOSPITAL - JERUSALEM   |
| Ref. No.   | رقم الشارة: 116/1/3 :  |
| Date:  | التاريخ: 20 حزيران 2021  |
|  | حضرة الدكتورة عائدة أبو السعود المحترمة  |
|  | مديرة دائرة التمريض والقبالة   |
| 401<br>X23   | كلية الطب وعلوم المسحة   |
|  | جامعة النجاح الوطنية   |
|  | نابلس  |
|  | تحية طيبة وبعد ،   |
|  | الموضوع : تسهيل مهمة بحث علمي<br>The Prevalence of Sepsis and Septic Shock:<br>t outcome among ICU Patients at a Tertiary Hospital in<br>Palestine<br>بالإشارة إلى كتابكم بتاريخ 2021/6/1 بخصوص تسهيل مهمة بحث طالبة الماجستير هدى ع   |
|  | متطلبات الحصول على درجة الماجستير .  |
| الم متشغ   |  |
| لإضافة لعدم نشر                                    | فإنه لا مانع لدينا من تسهيل مهمة الطالبة ، على أن يتم التنسيق مع مدير دائرة التمريض في<br>بخصوص جمع البيانات والمعلومات المطلوبة ، على أن يتم تزويد الإدارة بنتائج البحث ، با/   |
|  | بخصوص جمع البيانات والمعلومات المطلوبة ، على أن يم تريب ، 2 أن المعلومات المطلوبة ،<br>البحث إلا بموافقة من إدارة المستشفى .   |
|  | وتفضلوا بقبول فانق الإحترام والتقدير ٢٠٠   |
|  | بنها شر هد د   |
|  | الدكتور عدنان فرهود  |
|  | المدين العام   |
|  | تسخة : مدير دائرة التعريض  |
| rusalem: P.O. Box 19481, Code                      |  |
| I-Tour/ Mount of Olives, Jerusale<br>1. 02-6270222 | em # 0. Box 22110 Code 01200 91190   |
| x: 02-6288392                                      | سی بی این اور ایر طریق<br>نیز این اورید. نشد می بی این 22110 (بر تربیدی) 91220 (بر تربیدی) 91200 (بر ت |

## **Appendix E**

## Permission from Makassed Hospital Ethics (Medical Research) Committee

Makassed Islamic Charitable Hospital – Jerusalem **Research Ethics Committee** Application for Ethical Approval of Research The research is scientifically sound Ves D No The research does not expose subjects to more than minimal risk Ves D No without the potential for direct benefit to them The confidentiality of personal health information and the privacy of Ves D No individuals are maintained Waiver of consent granted Yes D No There is an adequate process for informed consent Ves D No Project Title: The prevalence of Spsis and Septit shock; Treatment outcomes among ICU patients at a tertiary hospital in palestine PRIMARY INVESTIGATOR (Must be a permanent staff member) Name: Dr Jarral Cadaumi · Employment #: Department/Division NUISing /Alnajah Signature: University. INVESTIGATOR(S) Name: Huda Salah Odeh Employment #: 14742. Department/Institution: Almakassed hospital signature auture I \ we request to be granted privileges to conduct research at Makassed Hospital. Agreed (Signed Paper). General Director Comments: For REC chairperson/ representative only: Check one The candidate has shown satisfactory and research granted. □ The candidate needs further research clarification: suggested REC Chairperson/rep: Advec to Condect the research of Date: 18.7.202 (Signature: Halfer Makassed H Signature: Halfer Jr. Haitham A Head Dept. Gi Makassed Hospita Dr. Haitham Al-Hassan r. Haitham Al-rise Head, Dept. GSV Surgery MAK-FAS-21 (1/01 - Sep-2015

## Appendix F

## **Tables of Study**

## Table F.1

Mortality among the three groups (none, sepsis, & septic shock)

|        |             |                          | SEPSIS     |              | _     |         |
|--------|-------------|--------------------------|------------|--------------|-------|---------|
| Status | Total       | None                     | Sepsis     | Septic shock | $X^2$ | P Value |
| Alive  | 959 (88.0%) | 874 (92.9%)              | 66 (76.7%) | 19 (30.2%)   | 230.8 | < 0.001 |
| Dead   | 131 (12.0%) | 0%) 67 (7.1%) 20 (23.3%) |            | 44 (69.8%)   | 230.8 | <0.001  |

### Table F.2

Binary logistic regression for mortality and characteristics

|              |       |      |       |         |        |       | C.I. for<br>P(B) |
|--------------|-------|------|-------|---------|--------|-------|------------------|
| Variable     | В     | S.E. | Wald  | P value | Exp(B) | Lower | Upper            |
| Sepsis       | -0.35 | 0.29 | 1.51  | 0.219   | 0.70   | 0.40  | 1.23             |
| Lactate      | 0.13  | 0.09 | 2.00  | 0.157   | 1.14   | 0.95  | 1.35             |
| CCI          | 0.20  | 0.10 | 4.07  | 0.044   | 1.22   | 1.01  | 1.49             |
| SOFA         | 0.26  | 0.05 | 24.24 | 0.000   | 1.30   | 1.17  | 1.44             |
| Age          | 0.00  | 0.01 | 0.00  | 0.974   | 1.00   | 0.98  | 1.02             |
| Gender       | 0.36  | 0.40 | 0.81  | 0.368   | 1.44   | 0.65  | 3.15             |
| SBP          | 0.01  | 0.02 | 0.05  | 0.826   | 1.01   | 0.96  | 1.05             |
| DBP          | -0.04 | 0.04 | 1.02  | 0.313   | 0.97   | 0.90  | 1.03             |
| LOS ICU      | 0.04  | 0.02 | 5.32  | 0.021   | 1.04   | 1.01  | 1.07             |
| LOS hospital | -0.03 | 0.02 | 3.00  | 0.083   | 0.97   | 0.95  | 1.00             |
| Constant     | -3.16 | 1.71 | 3.42  | 0.064   | 0.04   |       |                  |

## Table F.3

Area under the curve of lactate, SOFA, and CCI in predicting mortality

|          |      |      |         | Asymptotic 95% Cl |                |  |
|----------|------|------|---------|-------------------|----------------|--|
| Variable | Area | S.E. | P value | Lower<br>Bound    | Upper<br>Bound |  |
| Lactic   | 0.72 | 0.03 | 0.000   | 0.66              | 0.78           |  |
| SOFA     | 0.85 | 0.03 | 0.000   | 0.80              | 0.90           |  |
| CCI      | 0.71 | 0.03 | 0.000   | 0.64              | 0.77           |  |

## Table F.4

| D' 1 '.'        | •          | C              | •         | 1   |                        |
|-----------------|------------|----------------|-----------|-----|------------------------|
| Binary logistic | regression | tor            | Sepsis    | and | <i>characteristics</i> |
| 20000 10000000  |            | $j \sim \cdot$ | o ep o to |     | 0.101.00000.001100     |

|              |       |      |       |         |        | 95% C.I. for<br>EXP(B) |       |
|--------------|-------|------|-------|---------|--------|------------------------|-------|
| Variable     | В     | S.E. | Wald  | P value | Exp(B) | Lower                  | Upper |
| Lactate      | 0.13  | 0.09 | 2.42  | 0.120   | 1.14   | 0.97                   | 1.35  |
| CCI          | 0.20  | 0.10 | 3.83  | 0.050   | 1.22   | 1.00                   | 1.48  |
| SOFA         | 0.25  | 0.05 | 23.16 | 0.000   | 1.29   | 1.16                   | 1.43  |
| Age          | 0.00  | 0.01 | 0.00  | 0.959   | 1.00   | 0.98                   | 1.02  |
| Gender       | 0.36  | 0.40 | 0.79  | 0.373   | 1.43   | 0.65                   | 3.13  |
| LOS ICU      | 0.04  | 0.02 | 4.91  | 0.027   | 1.04   | 1.00                   | 1.07  |
| LOS hospital | -0.03 | 0.02 | 3.26  | 0.071   | 0.97   | 0.94                   | 1.00  |
| SBP          | 0.01  | 0.02 | 0.26  | 0.614   | 1.01   | 0.97                   | 1.06  |
| DBP          | -0.04 | 0.04 | 1.00  | 0.316   | 0.97   | 0.90                   | 1.03  |
| Constant     | -3.83 | 1.62 | 5.61  | 0.018   | 0.02   |                        |       |

#### Table F.5

Area under the curve of lactate, SOFA, and CCI in predicting sepsis

|          |      |      |         | Asymptotic 95%<br>Confidence<br>Interval |                |
|----------|------|------|---------|--|----------------|
| Variable | Area | S.E. | P value | Lower<br>Bound                           | Upper<br>Bound |
| SOFA     | 0.73 | 0.03 | 0.000   | 0.67                                     | 0.79           |
| CCI      | 0.70 | 0.03 | 0.000   | 0.64                                     | 0.76           |
| Lactate  | 0.46 | 0.03 | 0.203   | 0.39                                     | 0.52           |



# الانتان والصدمة الانتانية: الانتشار والعلاج والنتائج بين مرضى وحدات العناية المركزة

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قدمت هذه الرسالة استكمالا لمتطلبات الحصول علي درجه الماجستير في العناية المكثفة للتمريض، من كلية الدراسات العليا، في جامعة النجاح الوطنية، نابلس- فلسطين.

# الانتان والصدمة الانتانية: الانتشار والعلاج والنتائج بين مرضى وحدات العناية المركزة اعداد هدى صلاح مجد عودة إشراف دكتور جمال قدومي

## الملخص

خلفية الدراسة: الصدمة هي حالة صحية شائعة بين المرضى وحدة العناية المركزة. حالياً لا يُعرف سوى القليل عن إنتشار تعفن الدم والصدمة الإنتانية ونتائجهما الصحية في المستشفيات الفلسطينية.

أهداف الدراسة: أجريت هذه الدراسة لوصف بأثر رجعي خلال العامين الماضيين معدل إنتشار تعفن الدم والصدمة الإنتانية والوفيات الناجمة عنهما في وحدة العناية المركزة للبالغين في مستشفى المقاصد في فلسطين.

**طريقة الدراسة**: تم إستخدام التصميم الوصفي الإرتباطي في الدراسة الحالية. أجريت الدراسة في مستشفى المقاصد في فلسطين والذي يقدم مجموعة واسعة من خدمات الرعاية الصحية. تضمنت أدوات جمع البيانات التفاصيل الاجتماعية والديموغرافية للمرضى، وأداة Sepsis لتشخيص تعفن الدم، ودرجات تقييم فثل الأعضاء المتسلسل، ومؤشر تشارلسون للاعتلال المشترك.

نتائج الدراسة: شملت الدراسة 1101 مريضاً. كان معدل إنتشار تعفن الدم والصدمة الإنتانية بين مرضى وحدة العناية المركزة 13.6%. كانت نتائج تقييم فشل الأعضاء المتسلسل أعلى بشكل ملحوظ بالنسبة للمرضى الذين يعانون من الصدمة الإنتانية مقارنة مع أولئك الذين يعانون من تعفن الدم والذين ليس لديهم تعفن الدم. كان معدل الوفيات بين مرضى وحدة العناية المركزة 12%. أظهر الانحدار اللوجستي الثنائي والمناطق الواقعة تحت تمييز منحنيات التشغيل المتلقي أن درجات تقييم فشل الأعضاء المتسلسل، ومؤشر تشارلسون للاعتلال المشترك، وفترة مكوث المريض في وحدة العناية المركزة مؤشرات مهمة في التبوء بالوفيات.

إستنتاجات الدراسة: أظهرت نتائج هذه الدراسة أن تعفن الدم والصدمة الإنتانية من الحالات الصحية الشائعة التي تهدد الحياة بين المرضى في وحدة العناية المركزة في فلسطين. كانت معدلات الوفيات أعلى بشكل ملحوظ عندما يصاب مرضى وحدة العناية المركزة بتعفن الدم والصدمة الإنتانية. أظهرت نتائج هذه الدراسة أنه يمكن التنبؤ بالوفيات من خلال درجات تقييم فشل الأعضاء المتسلسل، ومؤشر تشارلسون للاعتلال المشترك، وفترة مكوث المريض في وحدة العناية المركزة. من بين هذه المتغيرات، تعتبر درجات تقييم فشل الأعضاء المتسلسل أقوى معيار تمييزي.

الكلمات المفتاحية: تعفن الدم، الصدمة الإنتانية، الإنتشار، وحدة العناية المركزة، المستشفيات، الوفيات. الوفيات.