

**KNOWLEDGE AND AWARENESS OF SEPSIS
AMONG ORTHOPAEDIC PATIENTS IN
HOSPITAL UNIVERSITI SAINS MALAYSIA
(HOSPITAL USM)**

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2020

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(HOSPITAL USM)**

by

NORSYAFIEKA AZIZ

**Dissertation submitted in partial fulfilment of the
requirements for the degree
of Bachelor of Nursing (Honours)**

June 2020

ACKNOWLEDGEMENT

First and foremost, I would like to express my greatest gratitude to Allah SWT for giving me the strength and guidance in completing the dissertation successfully. A special thank you goes to my lovely and supporting supervisor, Cik Norazliah Bt Hj Samsudin for spending her invaluable time and full support in guiding, supervising and encouraging me throughout the preparation until completion of the dissertation. At the same time, a lovely thanks to my co-supervisor, Dr Nur Syahmina Bt Rasudin for her guidance especially in the statistical part as it does help me a lot in order to analyse the result of this study, without their assistance and dedicated involvement along the process, this dissertation would have never been accomplished.

Furthermore, the most special and important gratitude to my parent. None of this could have happened without them. Thank you for the endless support and encouragement. They are my truly backbone and my source of inspiration to succeed and to finish this research project. Finally, I would like to thank you all the participants, my colleagues and lecturers for their support, advice and recommendations in preparing this dissertation. All the hard work and cooperation from everybody involved in my study either directly or indirectly are very gratefully acknowledged.

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LIST OF ABBREVIATION

HOSPITAL USM	-	Hospital Universiti Sains Malaysia
SIRS	-	Systemic Inflammatory Response Syndrome
CDC	-	Center for Disease Control
US	-	United States
ICUs	-	Intensive Care Units
SCCM	-	Society of Critical Care Medicine
HIV	-	Human Immunodeficiency Virus
SOFA	-	Sepsis-Related Organ Failure
PCT	-	Procalcitonin
CRP	-	C-reactive Protein
AMI	-	Acute Myocardial Infection
WHO	-	World Health Organization
ARDS	-	Acute Respiratory Distress Syndrome
HBM	-	Health Belief Mode
MCO	-	Movement Control Order

**PENGETAHUAN DAN KESEDARAN TERHADAP JANGKITAN KUMAN
DALAM KALANGAN PESAKIT ORTOPEDIK DI HOSPITAL UNIVERSITI
SAINS MALAYSIA**

ABSTRAK

Asepsis boleh menyebabkan kematian akibat jangkitan kuman dan salah satu kecemasan medikal yang memerlukan pengenalan awal. Objektif kajian adalah untuk mengetahui tahap pengetahuan dan kesedaran sepsis di kalangan pesakit ortopedik di Hospital USM. Kajian ini juga mengkaji perkaitan pengetahuan sepsis dengan jantina dan tahap pendidikan. Sebanyak 74 pesakit ortopedik yang dimasukkan ke hospital direkrut dalam kajian ini menggunakan kaedah persampelan rawak mudah. Data dikumpulkan dari Disember 2019 hingga Februari 2020 menggunakan soal selidik yang dikendalikan sendiri dan dianalisis menggunakan SPSS versi 23.0. Statistik deskriptif digunakan untuk dianalisis untuk mean, SD, frekuensi, peratusan dan Pearson's Chi Square. Kelulusan etika diperoleh daripada Jawatankuasa Etika Penyelidikan Manusia (JEPeM) USM. Hasil kajian menunjukkan bahawa tahap pengetahuan sepsis secara keseluruhan di kalangan pesakit ortopedik berada pada tahap tinggi dengan $M = 21.797$, $SD = 5.221$. Tahap kesedaran sepsis secara keseluruhan di kalangan pesakit ortopedik di Hospital USM berada pada tahap yang lebih tinggi dengan $M = 3.351$, $SD = 0.783$. Kajian mendapati bahawa jantina tidak berkait rapat dengan tahap pengetahuan sepsis ($p = 0.184$). Walau bagaimanapun, tahap pendidikan mempunyai kaitan yang signifikan dengan skor pengetahuan sepsis di kalangan pesakit ortopedik ($p = 0.05$). Hasil kajian ini dapat digunakan sebagai maklumat dasar untuk menentukan dan meningkatkan tahap pengetahuan dan kesedaran terhadap pencegahan sepsis sama ada di kalangan pesakit ortopedik atau pesakit lain.

**KNOWLEDGE AND AWARENESS OF SEPSIS AMONG ORTHOPEDIC
PATIENTS IN HOSPITAL UNIVERSITI SAINS MALAYSIA**

ABSTRACT

Asepsis can cause mortality due to the infection and one of the medical emergencies that need early identification. The objectives of study were to determine the level of knowledge and awareness of sepsis among orthopaedic patients in Hospital USM. This study also examined the association of knowledge of sepsis with gender and level of education. A total of 74 orthopedic patient who were hospitalized were recruited in this study using a simple random sampling method. Data were collected from December 2019 to February 2020 using self-administered questionnaires and analysed using SPSS version 23.0. Descriptive statistics was used to analysed for mean, SD, frequency, percentage and Pearson's Chi Square. Ethical approval was obtained from Human Research Ethics Committee (JEPeM) of USM. The findings revealed that overall knowledge level of sepsis among orthopaedic patient was at high level with $M=21.797$, $SD=5.221$. Overall level of awareness of sepsis among orthopaedic patients in Hospital USM were at higher level with $M=3.351$, $SD=0.783$. The study found that gender was not significance association with level of knowledge of sepsis ($p=0.184$). However, level of education was significant association with score of knowledge of sepsis among orthopaedic patients ($p=0.05$). The result of this study can be used as a baseline information to determine and improves level of knowledge and awareness towards sepsis prevention either among orthopaedic patients or other patients.

CHAPTER 1

INTRODUCTION

1.1 Background of study

Sepsis is defined as a systemic inflammatory response syndrome (SIRS) due to the infection and the patient experience more than two criteria: abnormal body temperature, heart rate, respiratory rate or blood gas or abnormal white blood cell count (Bone et al., 1992). Sepsis is a serious medical condition that clarifies as life-threatening organ dysfunction originates by a dysfunction of the host reaction to the infection (Hajj, Blaine, Salavaci, & Jacoby, 2018). Previously, studied of *Incidence and Impact of Organ Dysfunction Associated with Sepsis* done by Bertrand Guidet, Philippe Aegerter, Remy Gauzit, Patrick Meshaka, and Didier Dreyfuss claimed that most common organ dysfunction associated with sepsis were respiratory, circulatory and renal. Finding from a randomized control trial also supported these finding (Guidet, Aegerter, Gauzit, Meshaka, & Dreyfuss, 2005).

Sepsis is a serious medical condition that has been reported as a burden to worldwide (Dellinger et al., 2013; Hajj et al., 2018; Kaukonen, Bailey, Suzuki, Pilcher, & Bellomo, 2014; Schmid et al., 2004; Sogayar et al., 2008; Vincent et al., 2014). Cost of each individual diagnosed with sepsis is expensive to treat and correlated with readmission rates (Hajj et al., 2018). Event of sepsis led to discharge to hospice facilities or 30-day readmissions (Dietz, Jones, Small, Gaieski, & Mikkelsen, 2017). Mayr et al. (2017) in a cohort study also demonstrated there is 30-day readmission after sepsis represents 49% of the US population (Genga & Russell, 2017). In a retrospective cohort study by Sun et al (2016) claimed that unplanned hospital readmission secondary to infection after an episode of sepsis is common (Sun et al., 2016). The utilization of total

parenteral nutrition, duration of antibiotics, prior hospitalization and lower hemoglobin at discharge are factors associated with hospital readmissions.

According to the previous study, sepsis and trauma have high morbidity, mortality and cause a high cost of care (Raymond et al., 2017). Statistics in 2007, recorded that severe sepsis caused more than 700,000 hospitalizations, 200,00 deaths and 24 billion dollars in hospital in the United States (Lagu et al., 2012). Based on the 2013 HCUP statistical state that the cost of care for the sepsis was the most expensive disease treated in US hospital, 23 billion (Torio, Ph, Andrews, & Ph, 2013).

Lidicker et al (2001) reported that the epidemiology and incidence of sepsis in the United States (US) approximately 750,000 cases occur per-year (70% cases receive care in the high-dependency unit such as ICU, intermediate care unit and coronary care unit). An episode of sepsis is the tenth highest cause of death (Anderson, Ph, Smith, Ed, & Statistics, 2014), death in non-cardiac intensive care units (ICUs) (Lagu et al., 2012) and trauma patients (Sobrino & Shafi, 2013). Report from Center for Disease Control (CDC) claimed that an episode of sepsis diagnosed in 1.5 million people in the US and causing the death of 250,000 individual (Hajj et al., 2018). High risk of mortality is reported due to the delay medical treatment (Bloos et al., 2017) and early intervention of sepsis in the emergency department and ICU can reduce mortality of sepsis (Levy et al., 2010). Rubulotta et.al (2009) reported that early recognition and treatment to sepsis patient are crucial to reducing mortality rate. However, insufficient knowledge on symptoms of sepsis can cause a delay in medical treatment and increase mortality rate (Eitze et al., 2018) as the signs and symptoms of sepsis unrecognize (Park et al., 2014). Thus, knowledge regarding symptoms of sepsis and the ability to seek emergency medical

treatment is important to initiate early treatment (Eitze et al., 2018) and reduce mortality rates.

1.2 Problem Statement

Sepsis is a most familiar, least recognized illness in both developed and developing country (Ullah et al., 2016) and a serious medical condition that genuinely overburdened the healthcare system. A study reported that sepsis incidence becomes a major concern worldwide (Kopczynska et al., 2018) due to the high morbidity, mortality and financial cost to the health system (Perner et al., 2017). The reason this study conducted is to gain knowledge, awareness, and insight into the magnitude of the incidence of sepsis among worldwide, prevalence was the most measured. Based on the studied before, prevalence can be interpreted as the number of persons with a certain disease as a proportion of the entire patient population, measured at a specific point in time or over a specific period of time (Vanderwee, Clark, Dealey, Gunningberg, & Defloor, 2007).

According to the previously published studies, the prevalence of sepsis has raised by 1.5% annually and the number of patients diagnosed with sepsis is expected to reach 1 million in 2020 (Dombrowskiy, Martin, Sunderram, & Paz, 2007; Huang & Reade, 2008; Martin, Mannino, Eaton, & Moss, 2003) Society of Critical Care Medicine (SCCM) and American College of Chest Physicians Consensus Conference claimed that sepsis is systemic inflammatory response syndrome caused by infection (Bone et al., 1992). Sepsis is the final common pathway to death due to the infection (Kissoon, Daniels, Van Der Poll, Finfer, & Reinhart, 2016) and has been reported that infection causes of death more than 10 million people per year while sepsis caused between 3 and 10 per 1000 people commonly in high-income countries (Sepsis & Fleischmann, 2016). In both North America and Europe, the prevalence of severe sepsis and septic shock has increased over

time (Huang & Reade, 2008; Martin et al., 2003) meanwhile United states reported that there were 760,00 cases of incidence of sepsis occur per year (Mayr, Yende, & Angus, 2014). The American College of Surgeons National Surgical Quality Improvement Program databased claimed that there are 10 times cases of sepsis and septic shock compared to the myocardial infarction and pulmonary embolism cases (Moore, 2010). Previous study on 2017 also stated that the development of sepsis and septic shock in orthopaedic trauma patients (1.6%) are higher than non-trauma patients (0.5%) (Lakomkin et al., 2017). The author also claimed that, commonly sepsis develops during postoperative with serious complication that associated with death and had intense effect on inpatient. These postoperative rates of septicaemia doubling result between 1997 and 2006. The other study reported that orthopaedic and trauma device-related infection is one of the major complications in modern trauma and orthopaedic surgery(Moriarty et al., 2016). These incidences related infection range from 0.7% to 4.2% and can be higher after operative fixation of closed low-energy fractures to more than 30% in complex open tibia fracture.

Based on the other studies reported that every year sepsis causes 18 million of people suffer and cause more than 5 million of them to die (Pundir, Coomarasamy, Pundir, & Coomarasamy, 2016) main causes of death in trauma patient (Sobrino & Shafi, 2013) and non-cardiac intensive care units (ICU) (Lagu et al., 2012). The mortality rate of severe sepsis in developed countries has been estimated between 28 and 50% cases with ranging from 15% patients in sepsis and 40-50% patients in septic shock (Martin, 2012) meanwhile there are 60-80% of mortality rate in developing countries including Pakistan (Vincent, 2012). There are more than 50 cases admitted in Hospital Universiti Sains Malaysia (Hospital USM) due to the orthopaedics related infection from January 2001 to December 2002 (Yusof & Yusof, 2004). They commonly admitted due to the

various orthopaedic infections such as chronic osteomyelitis, pin tract infection, infected implants, traumatic and surgical wound infection.

Due to the worldwide incidence of sepsis and impact on the healthcare system, there are many studies conducted aiming to increase awareness and knowledge of the public on sepsis. However, there has been no published study regarding awareness and knowledge of sepsis in Malaysia among orthopaedic patients.

Awareness and knowledge on sepsis is a vital issue that needs to focus nowadays as the incidence of sepsis is responsible for the increase of mortality rate. Knowledge of early clinical manifestation of sepsis is pivotal in seeking early treatment. However, lack of knowledge and awareness of sepsis can lead to a delay in medical treatment (Eitze et al., 2018). Every delay in seeking treatment associated with an increase of mortality rate of sepsis by 2% for the delay in anti micro-biological treatment and 1% for the delay in source control (Bloos et al., 2017).

1.3 Research Questions

- I. What is the level of knowledge of sepsis among orthopaedic patients in Hospital Universiti Sains Malaysia (Hospital USM).
- II. What is the level of awareness of sepsis among orthopaedic patients in Hospital Universiti Sains Malaysia (Hospital USM).
- III. Is there any difference between gender and score of knowledge of sepsis among orthopaedic patients in Hospital Universiti Sains Malaysia (Hospital USM).
- IV. Is there any association between educational level and score of knowledge of sepsis among orthopaedic patients in Hospital Universiti Sains Malaysia (Hospital USM).

1.4 Research Objective

1.4.1 General Objective

To study the level of knowledge and awareness of sepsis among orthopaedic patients in Hospital Universiti Sains Malaysia (Hospital USM).

1.4.2 Specific Objectives

- I To determine the level of knowledge of sepsis among orthopaedic patients in Hospital Universiti Sains Malaysia (Hospital USM).
- II To determine the level of awareness of sepsis among orthopaedic patients in Hospital Universiti Sains Malaysia (Hospital USM).
- III To determine the difference between gender and score of knowledge of sepsis among orthopaedic patients in Hospital Universiti Sains Malaysia (Hospital USM).
- IV To determine association between educational level and score of knowledge of sepsis among orthopaedic patients in Hospital Universiti Sains Malaysia (Hospital USM).

1.5 Hypothesis

Hypothesis I : There is no difference between gender and score of knowledge of sepsis among orthopaedic patients in Hospital Universiti Sains Malaysia (H₀).

: There is difference between gender and score of knowledge of sepsis among orthopaedic patients in Hospital Universiti Sains Malaysia (H_A).

Hypothesis II : There is no association between educational level

and score of knowledge of sepsis among orthopaedic patients in Hospital Universiti Sains Malaysia (H0).

: There is association between educational level and score of knowledge of sepsis among orthopaedic patients in Hospital Universiti Sains Malaysia (HA).

1.6 Conceptual/ Operational Definitions

Definitions for the conceptual terms use in this research proposal are as follow:

Knowledge of sepsis

Knowledge on sepsis is defined as the facts, information, and skill acquired through experience, education: the theoretical or practical understanding of a subject(“Oxford University Press,” 2018).

Awareness of sepsis

Awareness on sepsis is defined as perception of a situation or facts or state of being aware and understanding something is happening and exists (“Oxford University Press,” 2018).

Thus, in this study knowledge and awareness on sepsis is about early clinical manifestation and the ability to seek emergency medical treatment (Eitze et al., 2018). Based on previous study, knowledge and awareness of sepsis referred on early recognition of clinical manifestation and the ability to seek emergency medical treatment. Thus, knowledge and awareness of sepsis in this study will be measured as Yes, No and Unsure in this instrument.

1.7 Significance of the study

Globally, the incidence of sepsis has been reported worldwide. Hence, in 2002, the Surviving Sepsis Campaign was launched to reduce global sepsis-related mortality (Slade, Tamber, & Vincent, 2003). Many types of research have been conducted aiming to increase awareness and knowledge of the public on sepsis either among public or healthcare providers. Nevertheless, the result of the study shown that both public and healthcare providers have low awareness and knowledge of sepsis. For example, an

international survey conducted in 2009 among 6021 participants from Europe and USA reported that 88% of the participants never heard the term of sepsis (Rubulotta et al., 2009) while the other studies revealed that the knowledge about sepsis diagnosis and management is lack among healthcare professionals (Assunção et al., 2010; Tufan et al., 2015). Thus, it shows that, early recognition of sepsis and the urge to seek early treatments influenced by many factors.

Study of knowledge and awareness of sepsis is very important, especially for the public to gain insight about the incidence of sepsis and its effect on the quality of life. Besides, the incidence of sepsis historically overburdened US healthcare system as it is overwhelmed with the cost of care during and post-hospitalization (Hajj et al., 2018). Consequences insufficient knowledge of sepsis can lead to a delay and medical treatment (Eitze et al., 2018). Based on the previous study claimed that cost of treatment for the sepsis accounted for 23 billion in US hospital and it is the most expensive treatment in the hospital (Torio et al., 2013) Thus, it is shown that every hour in sepsis treatment is vital to reduce overburdened to healthcare treatment. Well said treatments and prevention of sepsis should be considered as a priority in the healthcare system.

Through this study, the researcher can explore the level of knowledge and awareness of sepsis among orthopaedic patients in Hospital Universiti Sains Malaysia. Even though there has been no published study regarding awareness and knowledge of sepsis in Malaysia, this study can be as an indicator to assess the level of knowledge and awareness about sepsis among orthopaedic patients. Thus, it gives a positive impact to the hospital services in Hospital Universiti Sains Malaysia

CHAPTER 2

LITERATURE REVIEW

2.1 Introduction

This chapter review the current literature related to knowledge and awareness of sepsis. Furthermore, this chapter also provide a detail description on operational/conceptual framework chosen for the proposed study.

2.2 Concept of Sepsis

2.2.1 Definition

Sepsis described as the presence of the SIRS criteria and presumed or proven infection meanwhile severe sepsis was interpreted as sepsis accompanied by acute organ dysfunction. (Mayr et al., 2014). Based on the studies, sepsis and severe sepsis (accompanied by acute organ dysfunction) (Huang & Reade, 2008) is a potentially life-threatening disorder which is increasing in frequency (Rubulotta et al., 2009)

2.2.2 Risk Factor of Sepsis

Sepsis is a common disease that can happen in a person who is at risk to develop the disease. Based on the research done by Mayr et al in 2014, proposed that older age , male gender, black race, people who experience infection, non-infectious conditions, such as burns, acute pancreatitis, and trauma and pre-existing chronic health conditions are vulnerable population that prone to develop severe sepsis(Mayr et al., 2014). The author also claimed that an individual who develop severe sepsis have at least one chronic health condition and commonly occur in individuals with chronic obstructive pulmonary disease, cancer, chronic renal and liver disease, and diabetes. There is strong evidence

claimed that obese patients are more vulnerable to infections and more susceptibility to develop serious complications of common infections (Falagas & Kompoti, 2006).

Based on the studies before, there is a higher incidence of severe sepsis among black patients compared to white patients (Eachempati, Hydo, Shou, & Barie, 2006; Marshall, 2014). This higher rate is because black patients more prone to develop infection-related hospitalization, organ dysfunction, diabetes and chronic kidney disease (Mayr et al., 2010). Meanwhile based on research conducted before sepsis more dominant in men compared to women (Huang & Reade, 2008; Sakr et al., 2013). Mayr et al. proposed that the role of oestrogens and androgens hormone in the body responsible in sepsis outcomes (Mayr et al., 2010). Other than that, abnormalities in the immune response also risk for infection and severe sepsis (Mayr et al., 2014). For example, human immunodeficiency virus (HIV) steadily increase in ICU over past few decades (Coquet et al., 2010) and most common develop sepsis (Greenberg, Lennox, & Martin, 2012; Japiassu, Amancio, Mesquita, Luz, & Grinsztejn, 2010; Kim et al., 2013). Sepsis cases also common in cancer patients (Williams et al., 2004) and contributed to 30% of all hospitalized cancer deaths. (Mayr et al., 2010). Genetic factor also have been discuss to explain variability in susceptibility and outcomes of infection diseases (Mayr et al., 2014).

A study by Sorensen and colleagues (Sørensen TI, Nielsen GG, Andersen PK, 1992) claimed that genetic factors is more important in outcomes of infectious diseases compared with cardiovascular disease (Mayr et al., 2014). Furthermore, environmental factor also plays a vital role in sepsis outcomes. Severe sepsis is more dominant in colder months, both in the UK (35% higher in winter than in summer) (Padkin et al., 2003) and US (17.7% higher in fall than in summer) (Danai, Sinha, Moss, Haber, & Martin, 2007). Mortality rate sepsis is more common in winter and genitourinary infections are

significantly more frequent in summer (Mayr et al., 2014). Based on study done by James Arwyn Jones and Andrew J Brent, the risk factor for sepsis are summarized as below (Arwyn-Jones & Brent, 2019) :

Risk factors for developing sepsis	
Increased risk of infection	<ul style="list-style-type: none"> • Environmental factors (hygiene, sanitation) • Susceptibility of individual organs to infection, e.g.: <ul style="list-style-type: none"> ◦ Chronic obstructive pulmonary disease, bronchiectasis – respiratory infections ◦ Lymphoedema, ulcers, psoriasis etc. – skin infections ◦ Indwelling foreign bodies – urinary catheters and urinary infections, IV lines and skin infections ◦ Recent trauma, surgery or invasive procedure
Impaired immune response	<ul style="list-style-type: none"> • Diabetes • Congenital immunodeficiency syndromes • HIV/AIDS • Neutropenia • Splenectomy/hyposplenism • Iatrogenic (corticosteroids, chemotherapy, biological agents) • Other chronic conditions (e.g. malnutrition, diabetes mellitus, malignancy)
Pre-existing organ dysfunction	<ul style="list-style-type: none"> • Increased risk of organ failure from reduced physiological reserve, e.g. heart failure, chronic respiratory disease, chronic kidney disease
Extremes of age	<ul style="list-style-type: none"> • Neonates and infants (immature immunity, limited physiological reserve) • Elderly patients (immune senescence, comorbidity)
Other genetic factors	<ul style="list-style-type: none"> • Ethnicity (incidence higher among some racial groups) • Sex (incidence higher among male patients) • Specific immune defects, e.g. defect in terminal complement pathway leading to increased risk of meningococcal sepsis
Infection management	<ul style="list-style-type: none"> • Delayed or inappropriate initial treatment of bacterial infections increases the risk of progression to sepsis

Figure 2.1 : Risk Factor for developing sepsis

2.2.3 Sign and Symptoms of Sepsis

Sepsis is a life-threatening medical emergency that demand initial diagnosis and urgent remedy hence knowledge is crucial, especially in major risk groups such as the elderly (Eitze et al., 2018). Nevertheless, sepsis syndrome is not globally aware by the public (Rubulotta et al., 2009) and does not have specific signs and symptoms (Park et al., 2014). Public should be acknowledge that sudden cognitive impairment, hypotension is early sign and symptoms of sepsis (Eitze et al., 2018) and a simple infectious disease

such as fever, malaise, mental changes, dehydration, and shortness of breath can lead to sepsis and mortality can be high in these cases (Park et al., 2014).

Based on the studies before, sign and symptoms visualize as worsening inflammation, starting with SIRS, and progress from sepsis to severe sepsis and septic shock (Mayr et al., 2014). Abnormal temperature, heart rate, respiratory rate, and white blood cell count indicate criteria for SIRS. SIRS is defined if two out of four these criteria met (Mayr et al., 2014). Criteria for sepsis were proposed include infection and presence of any of the diagnostic criteria shown below (Levy et al., 2003) :

Term	Criteria
Sepsis	Documented (or suspected) infection with any one of the following clinical or laboratory criteria
General parameters	Fever, hypothermia, tachycardia, tachypnea, altered mental status, arterial hypotension, decreased urine output, significant peripheral edema, or positive fluid balance
Inflammatory parameters	Leukocytosis, leukopenia, hyperglycemia, increased C-reactive protein, procalcitonin, or creatinine, coagulation abnormalities, increased cardiac output, reduced mixed venous oxygen saturation
Hemodynamic parameters	Hypotension, elevated mixed venous oxygen saturation, elevated cardiac index
Organ dysfunction parameters	Arterial hypoxemia, acute oliguria, increase in creatinine level, elevated international normalized ratio or activated partial thromboplastin time, ileus, thrombocytopenia, hyperbilirubinemia
Tissue perfusion parameters	Hyperlactatemia, decreased capillary refill, or mottling

Figure 2.2 : Sign and symptoms of sepsis

2.2.4 Microbial Agent of Sepsis

Infection of sepsis were claimed due to the pathogenic gram-negative and positive bacteria, fungi and yeast (Carrigan, Scott, & Tabrizian, 2004a). However, prevalence of sepsis cause by Gram-positive organisms have increased in frequency over time and are now as common as gram-negative infections (Brun-Buisson, Doyon, & Carlet, 1996; S. Finfer et al., 2004; Marshall, 1999; Martin et al., 2003).

Previous study claimed that Staphylococci bacteria is the most common species in orthopaedic related infection (Moriarty et al., 2016). These incidence accounts for 20% and 30% of cases of infection after fracture fixation and prosthetic joint infection. Meanwhile, based on study done in Hospital Universiti Sains Malaysia (Hospital USM) in 2004, Staphylococcus aureus infection remains the most common organism causing musculoskeletal infection (Yusof & Yusof, 2004).

Based on the study before, statistics incidence of sepsis case due to the microbial agent in the United States rise annually with 13.7% per year: 52.1% gram-positive, 37.5% gram-negative, 4.7% polymicrobial, 4.6% fungal, and 1.0% anaerobic bacteria and surprisingly gram-positive infections increased annually at a mean rate of 26.3% per year over the study period (Martin et al., 2003). Increasing in the prevalence of sepsis incidence is due to the pathogen resistant to antimicrobial agents (Carrigan et al., 2004a) and increased nosocomial infections from varies sources. For example, catheterization and immunosuppressive therapies (Van Amersfoort, Van Berkel, & Kuiper, 2003) and is particularly alarming considering that reported rates of methicillin-resistant Staphylococcus aureus isolates range from 29% to 45% and demonstrate an increasing trend (Carbonne et al., 2002; FRANKLIN & LOWY, 1998; Wyllie, Peto, & Crook, 2005). Initial site of infection are respiratory tract infections (40–44% of cases), genitourinary infections (9–18% of patients) and intraabdominal infections (9–14%) (Huang & Reade, 2008; Zilberberg, Shorr, Micek, Vazquez-Guillamet, & Kollef, 2014).

2.2.5 Sepsis and Quality of life

Globally , severe sepsis is defined associated with acute organ failure (Bone et al., 1992) and supported by sepsis-related Organ Failure (SOFA) score by Vincent and colleagues (Marshall, 1999). Organ dysfunction need to be detected in order to meet

severe sepsis criteria and must be treated initially (Linde-zwirble & Angus, 2004) in order to prevent further complication. Previous study mentioned that implication of organ failure is the strongest predictor of death, both in terms of the number of organs failing and the degree of organ dysfunction (Mayr et al., 2014).

Based on study done by Bertrand Guidet and colleagues in 2005, the result of the study shows that common organ dysfunction were respiratory, circulatory and renal and majority of patients with severe sepsis develop more than two organ dysfunction (Guidet et al., 2005). Furthermore, the result of the study also proposed that, pulmonary, abdominal and cardiovascular are most common sites of infection due to the Staphylococcus and Pseudomonas species. Previous study stated that elderly survivors of severe sepsis three times more likely to develop persistent cognitive and functional impairments compared with elderly controls not hospitalized for sepsis (Iwashyna, Ely, Smith, & Langa, 2010). Based on statistics in Ministry of Health of Singapore in 2009, at least 17% of all deaths in Singapore were due to sepsis from pneumonia and urinary tract infection while 8% were due to cerebrovascular disease. Most common site of infection such as respiratory tract infections and pneumonia associated with the highest mortality rate (Esper et al., 2006).

Syndrome of severe sepsis and septic shock shows more severe results because of its progressive development of organ dysfunction with or without hypotension (Rubulotta et al., 2009). For example, severe sepsis and septic shock caused circulatory abnormalities (intra-vascular volume depletion, peripheral vasodilatation, myocardial depression, and increased metabolism). Hence it cause imbalance between systemic oxygen delivery and oxygen demand lead to the global tissue hypoxia or shock (Beal & Cerra, 1994).

2.2.6 Biomarkers

Early detection and immediate resuscitation of trauma and sepsis patients are crucial to prevent multi-organ failure and decrease mortality rate (Belletti et al., 2016; Cudnik, Newgard, Sayre, & Steinberg, 2009; Demetriades et al., 2006; Levy et al., 2015; MacKenzie et al., 2006). Hence, biomarkers are essential to diagnose or facilitate early diagnosis of sepsis in trauma patients (Ciriello et al., 2013). Biomarkers procalcitonin (PCT) and C-reactive protein (CRP) are used for sepsis diagnosis (Levy et al., 2003). However, there is strong proof stated that PCT was found to be effective in early identification of post-traumatic septic course and its use is suggested in clinical practice (Ciriello et al., 2013).

Delayed in diagnosis and provide antimicrobial intervention is the most common avoidable error in sepsis related mortality (Hotchkiss & Karl, 2003). Implication of failure to diagnose, delayed pathogen management and treatment correlate with increase a patient's risk of infection-related mortality (Carrigan, Scott, & Tabrizian, 2004). For instance, due to the delayed diagnosis and pathogens identified, 59% of isolated infections are nosocomial, which show higher correlation with inadequate treatment (Ibrahim, Sherman, Ward, Fraser, & Kollef, 2000). Thus, the ability of effective biomarkers to detect sepsis and ability off physicians to recognize and diagnose septic are vital in reducing mortality rate (Raymondos et al., 2012).

2.2.7 Management of Sepsis

Initial medical treatments are crucial as delayed in the medical treatment correlated with an increase of mortality risk by 2% of delay in antimicrobial treatment and 1% delay in source control (Bloos et al., 2017). Infection management which are manage source of control, administer effective antimicrobial agents against the pathogen

(Zanotti-Cavazzoni, Dellinger, & Parrillo, 2008) and administer antibiotics that often delayed (Pinel, Thievent, Wenzel, Auckenthaler, & Suter, 1996) and lead to system failure (Iregui, Ward, Sherman, Fraser, & Kollef, 2002). Patient with severe sepsis can be administer with effective antibiotics within 1 hour of diagnosis (Dellinger et al., 2004) to prevent further complication and can cause mortality (A. Kumar et al., 2006). Quality of choosing antibiotics depends on criteria below (Zanotti-Cavazzoni et al., 2008) :

- Probable pathogens, based on clinical diagnosis and source of infection (For example, pneumonia, bloodstream infection, abdominal source)
- Site where infection was acquired (community vs. hospital)
- Results obtained from diagnostic tests such as Gram staining
- Resistance patterns of local and hospital bacterial flora
- Patient comorbidities, drug allergies, and previous anti- biotic exposure

Another vital element of sepsis treatment is fluid resuscitation combine with antimicrobials and vasopressors(A. Kumar et al., 2006). Surviving Sepsis Campaign 2016 proposed that recommendation for fluid therapy administration of intravenous crystalloid, 30 mL/kg within 3 with combination of albumin into crystalloids if substantial amounts of crystalloids are required for initial resuscitation(Rhodes et al., 2017).

Delayed in administration of antibiotics and fluids resuscitation in severe sepsis (Dellinger et al., 2013; A. Kumar et al., 2006; Rivers et al., 2001) can worse patient's

outcome and inadequate treatment also can increase the risk of side effects (Carrigan et al., 2004a) Hence, every hour in sepsis management is vital (Eitze et al., 2018).

2.2.8 Demographic data towards awareness and knowledge of sepsis

In order to design optimal health education provisions, it is crucial to assess perceptions of elderly as the major risk group for sepsis and identify the relevant knowledge gaps (Rossmann, 2017) and the determinants of knowledge.

Previous study stated that knowledge is determine based on two categories which are sociodemographic variables (Beier & Ackerman, 2003)and health information sources (Geana, Kimminau, & Greiner, 2011; O’Keefe, Boyd, & Brown, 1998). Based on the study conducted by Eitze and colleagues, low, middle and high educational level (Schneider, 2008)), occupational status, rural or urban area, health insurance status, age and gender are used to determine sepsis knowledge. Eitze (2018) clarified that sources of health information, younger age and higher education also determine the sepsis knowledge. Hence, in the study, she identified educational level, age and how often the participants used sources of health information. Such as doctors, therapists, caregivers and classical media such as magazines, newspapers, radio and television, internet and pharmacists (Eitze et al., 2018). Based on the survey, an increase in knowledge was predicted by younger age ($\beta = - 0.169, p < 0.001$), higher education ($\beta= 0.166, p < 0.001$) and rural residence ($\beta = - 0.079, p = 0.039$). The only significant source of sepsis information was pharmacists ($\beta =0.128, p = 0.001$) (Eitze et al., 2018).

2.2.9 Knowledge and Awareness towards Sepsis

The ability of the public to recognize and familiar with the symptoms of sepsis is associate with the knowledge about the syndrome of sepsis and thus they will initiate medical treatment when it is most treatable (Rubulotta et al., 2009). Hence ,the timing of

presentation to the hospital and initiate medical treatment is likely more crucial in patients with sepsis (de Groot et al., 2015). Nevertheless, based on the previous study shows that, there are still lacking knowledge and awareness about sepsis among public.

Based on study by Rubulotta et al (2009) done in Europe (5021 people), France (1007), Germany (1004), Italy (1003), Spain (1015), United Kingdom (1003) and in the United States (1000), the result showed that the percentage of the interviewed who knew of the term sepsis was very low which are five of the six countries, ranging from 4% in France to 19% in the United States. Meanwhile, 53% of those public in Germany had heard of the term sepsis and 81% of the United States population have never heard of the term sepsis.

Meanwhile, study of awareness of sepsis in the general Korean population was conducted and the results is compared with the knowledge of AMI and stroke (Park et al., 2014). However, the result shows that public awareness and knowledge regarding sepsis are poor compared with AMI and stroke in the general Korean population. From 1,081 participants in the survey, 1,019 participants (94.3%) had heard of the term AMI, and 1,047 participants (96.9%) had heard of the term stroke. Oppositeness, only 831 (76.9%) from them had heard the term sepsis and 295 (35.0%) knew the correct definition of sepsis. This significantly shows that, awareness and knowledge of AMI and stroke are higher than the awareness and knowledge of sepsis in the general Korean population (chi-square test, $P < 0.05$). Hence, the overall awareness of sepsis in the general Korean population was 27.3% (295/1,081) out of 1081 participants. 601 respondents (72.3%) out of 831 respondent who had term of sepsis claimed that, they had heard the term sepsis from public media and internet. Meanwhile, from 831 respondents who had heard of the

term sepsis, 114 participants (10.5%) proposed that sepsis is a transmitted disease while 191 (17.7%) responded had no knowledge of transmissibility (Park et al., 2014).

Other random telephone survey conducted in 1067 respondent to assess public awareness of sepsis and stroke in Singapore (Phua, Lim, Tay, & Aung, 2013). Out of 1067 respondent, only 5.0% of respondents had heard of the term sepsis with 4.2% could provide at least one accepted definition and 90.3% of respondents had heard of the term stroke with 76.7% could name at least one accepted warning sign, and 75.5% could name at least one accepted risk factor. The result of the survey significantly present that the public awareness of stroke better than sepsis.

Based on a study carried by Eitze and colleagues shows that overall awareness of sepsis, the understanding of its risk factors, symptoms and prevention is low in the German and Thuringian especially among elderly (Eitze et al., 2018). Furthermore, high-risk groups like elderly are not aware that vaccination protects against sepsis (Hegarty, Tan, O'Sullivan, Cronin, & Brady, 2000). Hence, knowledge about early sign and symptoms of sepsis, recognition and prevention of sepsis through vaccination are crucial especially among elderly (Eitze et al., 2018)

Even though syndrome of sepsis does not show specific signs and symptoms, the public should be aware and recognize that a simple infectious disease such as fever, malaise, mental changes, dehydration, and shortness of breath can lead to sepsis and mortality rate can be increase (Park et al., 2014). Hence, Park and colleagues mention that awareness and knowledge of sepsis are important and crucial to initiate early medical treatment. Such knowledge about early sign and symptoms of sepsis is necessary for the public to recognize sepsis, and thus reduce mortality rate by seeking medical treatment earlier (Rubulotta et al., 2009). Thus, initial medical treatment will improve patient's

outcome, yet treatment may be delayed if the patient does not present them self for medical care until late in the disease process. The author also proposed that, lack of public knowledge about early symptoms of sepsis proportionately due to the small amount of resources put into research in the area. Hence, collaboration with the media to acknowledge public about the syndrome of sepsis and complexity of sepsis may be an important early step in the efforts to decrease mortality in each country (Rubulotta et al., 2009).

2.2.10 Sepsis among Orthopaedic patients

Incidence of sepsis during postoperative is a common cases and those cases has been documented by countless studies in the general medical as well as orthopaedic literature, with postoperative rates of septicaemia cases repeated between 1997 and 2006 (Malina, 2010; Mokart et al., 2005; Vogel, Dombrovskiy, Carson, Graham, & Lowry, 2010). Sathiyakumar et al. demonstrated that patients with orthopaedic trauma and hip fracture (Sathiyakumar et al., 2015) tend to experience complexity of sepsis included many other complications (Lakomkin et al., 2017). An orthopaedic surgeon declared that orthopaedic trauma patient more susceptible to develop postoperative sepsis compared to those undergoing nontraumatic procedures (Lakomkin et al., 2017) as traumatic injury caused an immune suppressive effect on the rest of the body, thus induce septicaemia (Ertel W, Keel M, 1996; Lakomkin et al., 2017). Lakomkin and the colleagues declare that the use of corticosteroids and hypertension can cause development of sepsis in orthopaedic trauma patient yet no study has examined septic complications (Lakomkin et al., 2017).

Orthopaedic surgery commonly focused on the diagnosis and treatment of musculoskeletal sepsis as infections most likely involving bones, joints, muscles, and

skin (Golubovska, Solovjova, Vigante, Miscuks, & Jurkevics, 2012). The author also claimed that, coxitis, gonitis, arthritis, spondylodiscitis and compartment syndrome are the common source of infection for musculoskeletal infection. Golubovska and colleagues state that most of infections caused by bacteria that have either entered the blood stream, other site, or were present in the skin and soft tissue. These bacteria can suppress patient's immune system, produce septicaemia and at the final state lead to septic shock and multiorgan dysfunction. At the meantime, various studies of basic science proposed that orthopaedic trauma and orthopaedic trauma injuries may be associated with immunosuppression that contributes to sepsis (Giannoudis et al., 1998, 2000; Smith et al., 2000; Wanner et al., 2000).

Another infection in orthopaedic patients are spinal infection (such as spondylitis and discitis) (Bettini, Girardo, Dema, & Cervellati, 2009; Gouliouris, Aliyu, & Brown, 2010) septic arthritis which are very serious condition that can cause fatality (Coakley et al., 2006) and iliopsoas abscess show unclear sign and symptoms (Croucher, 2014). Hence, once the abscess or pus is discharge and detected, other than early diagnosis successful treatment should include aggressive surgical drainage and proper antibiotic use (Ebraheim, Rabenold, Patil, & Sanford, 2008; Garner, Meiring, Ravi, & Gupta, 2007). Fever, pain and limitation of movement are example of classic symptoms of orthopaedic inflammation that not presented in all patients (Golubovska et al., 2012).

However, out of all of this incidence, the development of sepsis or septic shock in orthopaedic trauma patients is still unclear (Lakomkin et al., 2017). Most finding of the existing studies suggest that unspecific diagnostic to orthopaedic surgery (Bateman, Schmidt, Berman, & Bittner, 2010; Mokart et al., 2005; Wafaisade et al., 2011) is the preoperative risk factor that associated with septicaemia (Lakomkin et al.,

2017). However, Lakomkin and the colleagues stated that, the relationship between orthopaedic trauma and sepsis and orthopaedic intervention remains undiscovered (Lakomkin et al., 2017).

2.2.11 Surviving Sepsis Campaign

Sepsis and severe sepsis are significantly an important public health problems that associated with high mortality (Mayr et al., 2014). Over the past 2 decades, incidence of septicaemia and mortality rate of septicaemia found increase in United States (G. Kumar et al., 2011; Martin et al., 2003) with an estimated annual healthcare cost of \$16.7 billion and leads to 120 000 deaths in (Carrigan, Scott, & Tabrizian, 2004b). Based on the previous studies in UK (Padkin et al., 2003) and Brazil (Silva et al., 2004), sepsis incidence in ICU were increase. Previous survey by Adhikari and colleagues based on data from the United States and the World Health Organization (WHO) propound that sepsis kills more than 11,000 people per day (Adhikari, Fowler, Bhagwanjee, & Rubenfeld, 2010; OMS, 2004). Poor medical diagnosis and deficient treatment of sepsis causes the incidence increase with little improvement in mortality statistics (Carrigan et al., 2004a).

Thus, public awareness regarding the seriousness of sepsis incidence and education of the high mortality of sepsis is important for public action (Park et al., 2014). European Society of Intensive Care Medicine, the SCCM, and the International Sepsis Forum in 2002 collaborated with an international effort to decrease the mortality of sepsis by 25% in 5 years. Intensive care professional societies launched a public and clinician educational effort which is Surviving Sepsis Campaign (Dellinger et al., 2004; Rubulotta et al., 2009; Slade, Tamber, & Vincent, 2003) that produced evidence based guidelines to assist in the treatment and management of severe sepsis and septic shock (Dellinger et

al., 2004, 2008). Information about the disease, early sign and symptoms of the disease, prompt presentation, the important to initiate early medical treatment and intervention that can improve the outcome should be included in the campaign public awareness (Kerns, Heidmann, Petty, & Prabhakaran, 2011). Other than that, National and international initiatives such as World Sepsis Day is held with the objective to increase awareness and knowledge about sepsis (Eitze et al., 2018).

Support from public also play an important role in increasing public awareness and improve the urge to approach medical treatment (Quale & Droller, 2007). Public media, internet, campaigns, education in schools, and education for patients and relatives are very beneficial and effective method to improve the public awareness of sepsis (Fogle et al., 2010; Luepker et al., 2000; Mellon, Hickey, Doyle, Dolan, & Williams, 2014).

Over the past 2 decades, the fatality incidence of sepsis has reduce due to advances in supportive care for the critically ill patients (Kuzniewicz et al., 2008). For example, since execution of Surviving Sepsis Campaign and low tidal volume of ventilation in patients with acute respiratory distress syndrome (ARDS), incidence of mortality rate among critically ill patients with severe sepsis has decreased (Brant & Fabisiak, 2013; S. R. Finfer, Vincent, Angus, & Van Der Poll, 2013; Kuzniewicz et al., 2008; Storgaard et al., 2013; Urtecho et al., 2013).

2.3 Theoretical/Conceptual framework of the study

In this study, the researcher will be use theory of Health Belief Mode (HBM) that was developed in 1950s by a group of U.S Public Health Service psychologist which are Hochbaum, Rosenstock and Kegels (Rosenstock, 1974) . This model is developed by them, to demonstrate why many people did not contribute in public health programs (Rosenstock, 1974), broad variety of health-related actions and give considerable support