A FIVE-YEAR REVIEW OF HEALTH CARE-ASSOCIATED INFECTIONS IN A TERTIARY BURN UNIT IN MALAYSIA

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TABLE OF CONTENT

LIST OF TABLES

LIST OF FIGURES

LIST OF ABBREVIATIONS

BWIs	Burn wound infections
CDC	Centers for Disease Control
HAIs	Hospital-Acquired Infections
ICU	Intensive Care Unit
IQR	Interquartile range
JEPeM	The Human Research Ethics Committee of Universiti Sains Malaysia
MREC	Medical Research and Ethics Committee
PBIs	Primary blood stream infections
SD	Standard deviation
SIRS	Systemic inflammatory response syndrome
SPSS	Statistical Package for Social Science
SSIs	Surgical site infections
UTIs	Urinary tract infections
WHO	World Health Organisation

LIST OF SYMBOLS

°C	degree Celsius
ε	expected difference between mean of with infection group and mean of without infection group
k	number of independent variables
n_1	sample size group 1 (with infection)
n_2	sample size group 2 (without infection)
p	smallest of the proportions of patients with or without infection
σ	standard deviation
$Z_{\alpha/2}$	z-score at α significance level (Type I error, for two-tailed hypothesis testing)
Z_{β}	z-score at β significant level (Type II error)

KAJIAN BERKENAAN JANGKITAN NOSOKOMIAL DI SEBUAH UNIT RAWATAN KEBAKARAN TERTIARI DI MALAYSIA SEPANJANG TEMPOH LIMA TAHUN

Abstrak

Pengenalan

Kadar jangkitan nosocomial dilaporkan dalam lingkungan 4.0 ke 11.9%. Pesakit-pesakit kebakaran lazimnya memerlukan jangka masa rawatan yang lama dan pelbagai prosedur invasif dan teraputik. Akibatnya, pesakit-pesakit ini mudah terkena jangkitan yang merupakan salah satu komplikasi yang memudaratkan. Data mengenai kejadian jangkitan nosokomial di kalangan pesakit-pesakit kebakaran di Malaysia adalah terhad. Oleh itu, kajian ini bermatlamat untuk menentukan kadar kelaziman dan faktor-faktor risiko untuk jangkitan nosokomial dikalangan pesakit-pesakit kebakaran akut di Unit Rawatan Kebakaran Hospital Kuala Lumpur sepanjang tempoh lima tahun.

Metodologi

Kajian ini melibatkan 219 pesakit yang berumur 12 tahun dan ke atas yang telah dimasukkan ke Unit Rawatan Kebakaran Hospital Kuala Lumpur untuk menerima rawatan luka kebakaran dari tempoh Januari 2016 hingga Disember 2020. Pesakit-pesakit tanpa data kajian yang lengkap seperti jangkitan nosokomial, umur, jantina, jenis, durasi dan sebab kebakaran dikecualikan dari kajian. Kadar jangkitan nosokomial diperolehi dengan mengira nisbah antara jumlah pesakit yang terkena jangkitan dengan jumlah keseluruhan pesakit. Model regresi logistic digunapakai untuk menilai faktor-faktor risiko untuk jangkitan nosokomial.

Keputusan

Kadar jangkitan nosokomial adalah 16.0% dengan selang keyakinan (CI) 95% (12% hingga 21%). 42.9% pesakit menghidap luka melecur, 26.0% luka kebakaran, 15.1% luka terma manakala 7.3% menghidap luka kebakaran sentuhan. Organisma yang menyebabkan jangkitan nosokomial tertinggi merupakan *Pseudomonas aeruginosa* (62.9%), *Acinetobacter baumanii* (11.4%), MRSA (8.5%) dan *Staphylococcus aureus* (5.6%). Kebanyakan jangkitan nosokomial berpunca dari luka kebakaran (74.3%), diikuti dengan jangkitan melalui darah (17.1%), jangkitan paru-paru (5.7%) dan jangkitan melalui air kencing (2.9%). Median tempoh kemasukan ke wad adalah 5 hari. Jangkitan nosokomial menyebabkan peningkatan ketara kepada tempoh kemasukan ke wad dengan penambahan 34 hari ($P<0.001$). Faktor-faktor risiko signifikan untuk jangkitan nosokomial termasuklah umur > 50 tahun, kemasukan ke wad > 14 hari dan jumlah luas permukaan luka kebakaran > 10%.

Kesimpulan

Kadar jangkitan nosokomial di Unit Rawatan Kebakaran Hospital Kuala Lumpur adalah lebih tinggi dari kadar yang pernah dilaporkan di negara-negara lain. Jangkitan nosokomial juga menyebabkan peningkatan ketara kepada tempoh kemasukan ke wad dengan penambahan 34 hari. Umur > 50 tahun, kemasukan ke wad > 14 hari dan jumlah luas permukaan luka kebakaran > 10% merupakan faktor-faktor risiko signifikan untuk jangkitan nosokomial. Oleh itu, kami ingin mengesyorkan langkah-langkah penambahbaikan dari segi pencegahan dan kawalan jangkitan serta protokol pengurusan yang lebih jelas berdasarkan data jangkitan tempatan bagi mengurangkan kadar kematian dan morbiditi akibat dari kecederaan kebakaran.

Kata kunci

Jangkitan nosokomial, luka kebakaran, Malaysia.

A FIVE-YEAR REVIEW OF HEALTH CARE-ASSOCIATED INFECTIONS IN A TERTIARY BURN UNIT IN MALAYSIA

Abstract

Introduction

Health care-associated infections (HAIs) range between 4.0 to 11.9%. Burn patients often require prolonged hospitalisations and multiple invasive diagnostic and therapeutic procedures. Consequently, patients contract infections which are the most potentially serious complications that occur. In Malaysia, there is limited data on the incidence of these HAIs among burn patients. This study therefore aims to determine the prevalence and risk factors for HAIs in acute burn patients at Hospital Kuala Lumpur, Malaysia, Burn Unit over a 5-year period.

Methodology

This was a retrospective cohort study that enrolled 219 patients aged 12 years and above who were admitted into the adult Burn Unit of Hospital Kuala Lumpur within 3 days following the burn injury from January 2016 until December 2020. Patients with incomplete data on key variables like HAIs, age, sex, nature and duration of injury and cause of injury were excluded from the study. The prevalence of HAIs was obtained as the proportion of patients who developed HAIs divided by all the patients enrolled into the study. A logistic regression model was used to assess for the risk factors for HAIs.

Results

The prevalence of HAIs was 16.0% with a 95% CI (12% to 21%). In this study, 42.9% of the participants had scalds, 26.0% had flame burns and 15.1% had burns due to thermal injuries while 7.3% were contact burns. The common causative organisms were *Pseudomonas aeruginosa* (62.9%), 11.4% had *Acinetobacter baumanii* (11.4%), MRSA (8.5%) and *Staphylococcus aureus* (5.6%). Among the patients who had HAIs, 74.3% had wound infections, 17.1% were blood infections and 5.7% were lung infections while only 2.9% had urine as their route of infection. The median hospital stay was 5 days and presence of HAI significantly increases hospital stay by 34 additional days ($P < 0.001$). Age of more than 50 years OR 2.39 (95% CI; 1.33 to 4.30, $P = 0.004$), duration of hospital stay of more than 14 days OR 6.79 (95% CI; 2.56 to 17.98, $P < 0.001$), and total burn surface area of more than 10% OR 5.10 (95% CI; 2.47 to 10.53 $P = <0.001$) were significant risk factors for HAIs.

Conclusion

The prevalence of HAIs in the adult Burn Unit of Hospital Kuala Lumpur was slightly higher than what has been reported in other countries and presence of HAIs increases hospital stay by 34 additional days. In addition, TBSA, age of more than 50 years and prolonged hospital stay were significant risk factors for development of HAIs. We therefore recommend improvements in preventive measures, improved infection control and a clear burn management protocol, based on local infection data so as to reduce the mortality and morbidity rates due to burn injuries.

Keywords

Health Care Associated Infections, burns, Malaysia.

CHAPTER ONE

INTRODUCTION

1.1 Introduction

Burns are a devastating public health problem worldwide and account for about 180,000 deaths annually. The World Health Organisation (WHO) estimates that around 11 million people require medical attention due to burn injuries each year (WHO 2018). The cost of treating these injuries along with their complications poses a financial burden to health care facilities with the hospital care cost for a burns patient ranging between 11 to 125,000 US dollars worldwide (Saavedra, De Oliveira Leal et al. 2021).

Burn patients are vulnerable to infections owing to the nature of the injury itself which causes the loss of the first line of defence against microbial invasion and alterations in the components of the immune system (Norbury, Herndon et al. 2016, Lachiewicz, Hauck et al. 2017). These patients often require prolonged hospitalisations and multiple invasive diagnostic and therapeutic procedures such as central venous and urinary catheter insertions (Ciofi Silva, Rossi et al. 2014) as per the management guidelines of burn patients (ACS 2022). These patients can contract infections which are one of the most potentially serious complications that occur (Zampar, Anami et al. 2017). Majority of death following burn injuries are attributed to these infections rather than burn shock and hypovolaemia (Bharwana, Farid et al. 2016). In Malaysia, there is limited data on the incidence of these health care-associated infections among burn patients.

In the last decade, there has been a substantial improvement in the survival rate for burn patients (Rafla and Tredget 2011, Strassle, Williams et al. 2017) evidenced by reduced mortality and days of hospital stay (Wang, Beekman et al. 2018). This is largely attributed to advances in fluid resuscitation, nutritional support, burn wound

care, infection control practices and intensive care management in specialised burn centres (Leseva, Arguirova et al. 2013, Shields, King et al. 2016). Even though some factors can be optimised, risk factors like inhalation injury and having total burn surface area of more than 10% have showed an association with healthcare associated infections (Strassle, Williams et al. 2017, Strassle, Williams et al. 2017). Other studies showed that burn mechanism especially flames and scalds, central venous catheter use, and ethnicity are associated with healthcare associated infections (Escandón-Vargas, Tangua et al. 2020). However, little is known about the risk factors for health care-associated infections in Malaysia.

This study therefore aims to determine the prevalence and risk factors for healthcare associated infections in acute burn patients receiving inpatient treatment at Hospital Kuala Lumpur, Malaysia, Burn Unit over a 5-year period.

1.2 Problem statement and rationale of the study

Health care-associated infections have been reported to range between 4.0 to 11.9% (Haque, Sartelli et al. 2018). These are mainly surgical site infections (SSIs), pneumonia, gastrointestinal infections, and bloodstream infection (Escandón-Vargas, Tangua et al. 2020). Urinary tract infections and ventilator-associated events have also been reported among others (Izadi, Eshrati et al. 2020). The HAIs consequently lead to prolonged hospital stay, inappropriate use of antibiotics and hence acquisition of multiple drug resistant infections (van Langeveld, Gagnon et al. 2017). Patients with HAIs have been reported to have larger burns percentages, higher death rates and required prolonged intensive care and hospital stays (Bharwana, Farid et al. 2016).

Due to the financial consequences of HAIs and prolonged hospital stay, it is important to know the most common HAIs among burn patients in Hospital Kuala Lumpur, Malaysia. Findings from this study will highlight the burden of HAIs among burn patients in our setting. In addition, studies have shown known risk factors associated with HAIs to be extensive burn injuries, age > 65 years, presence of inhalational injury and presence of invasive devices (Strassle, Williams et al. 2017). However, there is scanty information on the risk factors of HAIs in our setting, yet these are important in order to review the management of patients at the Burn Unit of Hospital Kuala Lumpur, Malaysia. Findings from this study will provide precious data that will be used to make improvements in preventive measures as well as treatment strategies in burn patients nationwide. A conscious burn management protocol, based on local infection data can positively affect the mortality and morbidity rates.

1.3 Objectives

1.3.1 General Objective

To determine the prevalence and risk factors associated with development of health care associated infection at the Hospital Kuala Lumpur Burn Unit.

1.3.2 Specific Objectives

1.3.2 (a) To determine the most common causative organism of health care-associated infection during the early and late stages of infection.

1.3.2 (b) To determine the most common site of infection during the early and late stages of infection.

1.3.2 (c) To determine the effect of health care-associated infection on duration of hospital stay

1.3.2 (d) To determine the risk factors associated with the development of health care-associated infections in burn patients.

1.4 Research questions

1.4.2 What is prevalence of health care associated infections at the Hospital Kuala Lumpur Burn Unit?

1.4.3 What are the most common causative organisms during the early and late stages of infection?

1.4.4 What is the most common site of infection?

1.4.5 Does health care-associated infection affect the length of hospital stay?

1.4.6 What are the risk factors associated with the development of health care-associated infection in burn patients?

1.5 Hypothesis

There is a high incidence of health care-associated infection at the Hospital Kuala Lumpur Burn Unit.

Null Hypothesis

There is a low incidence of health care-associated infection at the Hospital Kuala Lumpur Burn Unit.

CHAPTER TWO

LITERATURE REVIEW

2.0 Literature review

Nosocomial infection

In 1988, the Centers for Disease Control (CDC) came up with a set of definitions for surveillance of nosocomial infections. The definitions included criteria for common nosocomial infections as well as infections that occur infrequently but have serious consequences (Greenhalgh, Saffle et al. 2007). Two decades later, the term "nosocomial" has been replaced by "health care-associated" (HAI), along with the elimination of certain points previously mentioned in the 1988 definitions and modifications in others (Horan, Andrus et al. 2008).

HAI is defined as a localised or systemic condition resulting from an adverse reaction to the presence of an infectious agent(s) or its toxin(s). There must be no evidence that the infection was present or incubating at the time of admission to the acute care setting. HAIs may be caused by infectious agents from endogenous (body sites normally inhabited by microorganisms) or exogenous sources such as patient care equipment and medical devices.

Local studies

Studies conducted on burns in Malaysia have been scarce. The earliest that can be found was the one conducted in 1987 by Ghani AN and Ibrahim SH, which reviewed the epidemiology of burn patients admitted to the General Hospital, Kuala Lumpur (Ghani and Ibrahim 1987). Back then, burn cases were managed by the Orthopaedics and Traumatology Department without a specialized burn unit. The incidence of infection was reported at a high rate of 57.1% with the most common organism being from the Staphylococcus group (36.6%). Septicemia was the cause of death in 7.4%

of the patients(Ghani and Ibrahim 1987). Chan KY et al. also did an epidemiological study on burn patients admitted to the Burn Unit of Hospital Universiti Kebangsaan Malaysia between October 1999 and November 2001. The mortality rate during the study period was 6.3% and main cause of death was inhalational injury (Chan, Hairol et al. 2002).

Tan Chor Lip et al. in 2019, investigated the risk factor for death in the severe burned patient and identified factors that predict burn mortality in order to formulate treatment plans that may improve patient survivability. Mortality rates were high in patients with TBSA > 20%, inhalational injury, early SIRS and ventilated patients. In this study, the mortality rate was 12.2%, with infection as the main cause in 39.6% of cases (Tan Chor Lip, Tan et al. 2019). None of the aforementioned studies focused on health care-associated infections in Burn Units.

Health Care-Associated Infections (HAIs) Worldwide

Review of infections in Burn Units have been conducted worldwide. Rates of HAIs have been reported from 4.0 to 11.9% (Haque, Sartelli et al. 2018).

Common pathogens include *Pseudomonas aeruginosa*, *Staphylococcus aureus* and *Acinetobacter baumanii*, with the latter being reported as an emergent cause of infection especially in tropical warm climates (Chim, Tan et al. 2007). In another study, 19 out of 53 patients had positive blood culture results of which 89.0% were *Pseudomonas aeruginosa* and overall mortality rate was reported to be 18.5% (Lari and Alaghehbandan 2000). Common types of infection include burn wound infections, primary blood stream infections, urinary tract infections and pneumonia, with different centers reporting different rates of occurrences (Santucci, Gobara et al. 2003).

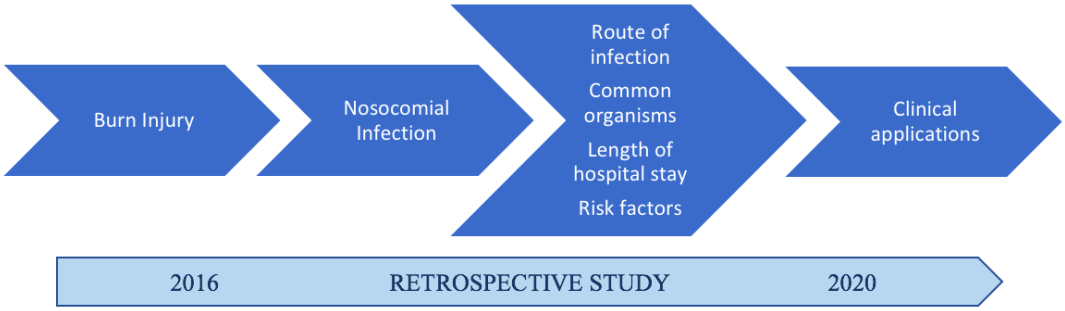
Factors associated with Health Care-Associated Infections (HAIs)

Known risk factors associated with HAIs are extensive burn injuries, age > 65 years, presence of inhalational injury and invasive devices (Strassle, Williams et al. 2017). Individuals more than 65 years of age are more susceptible to severe burn injury and hence increased risk of mortality (Romanowski and Sen 2022). Prolonged hospital stay is reported as a risk factor for acquisition of multidrug resistant infection. Likewise, patients who develop multidrug resistant infections are at a high risk of death and prolonged hospital stay (Peters, Olson et al. 2019). Patients with HAIs have been reported to have larger burns percentages, higher death rates and required prolonged intensive care and hospital stays (Hwee, Song et al. 2016). Studies have also shown that 88.0% of burn patients who required intubation developed health care-associated infections (Wurtz, Karajovic et al. 1995). Burn patients who are intubated are at a higher risk of developing health care-associated infections as opposed to those who are not intubated.

CHAPTER THREE

METHODOLOGY

3.1 Conceptual framework



3.2 Research design

This was a retrospective cohort study comprising of patients admitted to the Burn Unit of Hospital Kuala Lumpur from January 2016 until December 2020 listed in the admissions census.

3.3 Study area

This study was conducted at the Burn Unit of Hospital Kuala Lumpur, the largest government tertiary referral Hospital in Malaysia. The burn unit has a total bed capacity of 11 beds, two of which are available for intensive care unit (ICU) patients. The unit also houses its own operating theatre to cater for the burn patients.

3.4 Study population

This study included all acute burn patients aged 12 years and above who were admitted to the Burn Unit of Hospital Kuala Lumpur from January 2016 until December 2020.

3.5 Subject criteria

3.5.1 Inclusion criteria

Acute burn patients aged 12 years and above who were admitted into the adult Burn Unit of Hospital Kuala Lumpur within 3 days following the burn injury from January 2016 until December 2020.

3.5.2 Exclusion criteria

3.5.2 (a) Incomplete data from patients' records, missing key variables like age, sex, nature and duration of injury, cause of injury and missing information on whether the patient developed HAIs or not.

3.5.2 (b) Case notes that were untraceable or missing.

3.5.2 (c) Patients with delayed presentation (presented to hospital more than three days following burn injury) or presented with infected wound.

3.6 Sample size and sampling

Based on specific objective 3:

Research hypothesis ($\alpha = 0.05, \beta = 0.20$):

H_0: There is no significant difference of mean length of stay between patients with and without health care-associated infection.

H_1: There is a significant difference of mean length of stay between patients with and without health care-associated infection.

Sample size calculation for the equality of two means is calculated using the expression [6]

$n_1 = n_2 = \frac{2\sigma^2(Z_{\alpha/2} + Z_\beta)^2}{\varepsilon^2}$ where,

$\sigma =$ standard deviation

$Z_{\alpha/2} =$ z-score at α significance level (Type I error, for two-tailed hypothesis testing)

$Z_\beta =$ z-score at β significant level (Type II error)

$\varepsilon =$ Expected difference between mean of with infection group and mean of without infection group

n_1 = sample size group 1 (with infection)

n_2 = sample size group 2 (without infection)

Available information:

$\sigma = 9.30$ (Öncül O, et al. 2013 [23])

$Z_{\alpha/2} = Z_{0.025} = 1.96$

$Z_\beta = Z_{0.20} = 0.84$

$\varepsilon = 17.00$

$$n_1 = n_2 = \frac{2\sigma^2(Z_{\alpha/2} + Z_\beta)^2}{\varepsilon^2}$$

$$= \frac{2\,(9.30)^2(1.96 + 0.84)^2}{(17.00)^2}$$

$$= 4.69$$

$$\approx 5 \text{ patients}$$

By expecting 20% non-response rate,

$n_1 = n_2 = \frac{5}{(1-0.2)} = 6.25 \approx 7$ patients

Adequate sample size to perform the test by achieving 80% of power at 5% significance level and expecting 20% of non-response percentage is 7 patients per group.

Based on specific objective 4:

Based on the study of Peduzzi et. al. [24], minimum required sample size for the study by multiple logistic regression analysis can be calculated by using the following expression (see https://www.medcalc.org/manual/logistic_regression.php):

$n = \frac{10k}{p}$ where,

k = number of independent variables

p = smallest of the proportions of patients with or without infection

Available information:

k = 5

p = proportion of patients without infection = 0.287 (Öncül O, et al., 2013 [23])

$n = \frac{10k}{p}$

$n = \frac{10\ (5)}{0.287}$

$n = 174.2$

$n = 175$ patients

By expecting 20% anticipated drop-out rate,

$n = \frac{175}{(1-0.2)} = 218.8$

$n = 219$ patients

Adequate sample size needed to fulfil the fourth objective is 219 patients.

Conclusion:

Based on both sample size calculation, minimum sample required for the study is 175 patients. Therefore, by considering 20% anticipated drop-out rate, the required sample size for the study is 219 patients.

From January 2016 until December 2020, a total of 709 admissions into the burn unit were recorded. After exclusion, the remaining number of patients fulfilling the criteria was 665. 219 participants were then selected out of the 665 patients using simple random sampling.

3.7 Research tool

All necessary information was gathered from the admissions book, burn admission proforma, nosocomial infection surveillance data and patient's hospital case notes.

3.8 Operational definition

From the patient's case note, information that was extracted are according to the operational definition as listed below:

Healthcare-associated infections (HAIs) [13]:

A localised or systemic condition resulting from an adverse reaction to the presence of an infectious agent(s) or its toxin(s). There must be no evidence that the infection was present or incubating at the time of admission to the acute care setting.

For the interest of this study, HAIs was grouped into four main classes: burn wound infections (BWI), primary blood stream infections (PBI), pneumonias and urinary tract infections (UTI) and diagnosis was as defined by the Centres for Disease Control (CDC), Atlanta.

Burn Wound Infection

Burn infections must meet at least *1* of the following criteria:

1. Patient has a change in burn wound appearance or character, such as rapid eschar separation or dark brown, black, or violaceous discoloration of the eschar, or oedema at wound margin *and* histologic examination of burn biopsy shows invasion of organisms into adjacent viable tissue.
2. Patient has a change in burn wound appearance or character, such as rapid eschar separation, or dark brown, black, or violaceous discoloration of the eschar, or oedema at wound margin *and* at least *1* of the following:
    a. organisms cultured from blood in the absence of other identifiable infection
    b. isolation of herpes simplex virus, histologic identification of inclusions by light or electron microscopy, or visualization of viral particles by electron microscopy in biopsies or lesion scrapings.
3. Patient with a burn has at least 2 of the following signs or symptoms with no other recognised cause: fever (>38°C) or hypothermia (<36°C), hypotension, oliguria (<20 cc/hr), hyperglycaemia at previously tolerated level of dietary carbohydrate, or mental confusion *and* at least *1* of the following:
    a. histologic examination of burn biopsy shows invasion of organisms into adjacent viable tissue
    b. organisms cultured from blood
    c. isolation of herpes simplex virus, histologic identification of inclusions by light or electron microscopy, or visualization of viral particles by electron microscopy in biopsies or lesion scrapings.

Pneumonia

Pneumonia is defined separately from other infections of the lower respiratory tract. The criteria for pneumonia involve various combinations of clinical, radiographic, and laboratory evidence of infection. In general, expectorated sputum cultures are not useful in diagnosing pneumonia but may help identify the etiologic agent and provide useful antimicrobial susceptibility data. Findings from serial chest x-ray studies may be more helpful than those from a single x-ray film.

Pneumonia must meet one of the following criteria:

1. Rales or dullness to percussion on physical examination of chest AND any of the following:
    a. New onset of purulent sputum or change in character of sputum
    b. Organism isolated from blood culture
    c. Isolation of pathogen from specimen obtained by trans-tracheal aspirate, bronchial brushing, or biopsy
2. Chest radiographic examination shows new or progressive infiltrate, consolidation, cavitation, or pleural effusion AND any of the following:
    a. New onset of purulent sputum or change in character of sputum
    b. Organism isolated from blood culture
    c. Isolation of pathogen from specimen obtained by trans-tracheal aspirate, bronchial brushing, or biopsy
    d. Isolation of virus or detection of viral antigen in respiratory secretions
    e. Diagnostic single antibody titre (IgM) or fourfold increase in paired serum samples (IgG) for pathogen
    f. Histopathologic evidence of pneumonia

3. Patient ≤12 months of age has two of the following: apnoea, tachypnoea, bradycardia, wheezing, rhonchi, or cough AND any of the following:
    a. Increased production of respiratory secretions
    b. New onset of purulent sputum or change in character of sputum
    c. Organism isolated from blood culture
    d. Isolation of pathogen from specimen obtained by trans-tracheal aspirate, bronchial brushing, or biopsy
    e. Isolation of virus or detection of viral antigen in respiratory secretions
    f. Diagnostic single antibody titre (IgM) or fourfold increase in paired serum samples (IgG) for pathogen
    g. Histopathologic evidence of pneumonia

4. Patients ≤12 months of age has chest radiologic examination that shows new or progressive infiltrate, cavitation, consolidation, or pleural effusion AND any of the following:
    a. Increased production of respiratory secretions
    b. New onset of purulent sputum or change in character of sputum
    c. Organism isolated from blood culture
    d. Isolation of pathogen from specimen obtained by trans-tracheal aspirate, bronchial brushing, or biopsy
    e. Isolation of virus or detection of viral antigen in respiratory secretions
    f. Diagnostic single antibody titre (IgM) or fourfold increase in paired serum samples (IgG) for pathogen
    g. Histopathologic evidence of pneumonia

Symptomatic urinary tract infection

A symptomatic urinary tract infection must meet at least 1 of the following criteria:

1. Patient has at least 1 of the following signs or symptoms with no other recognized cause: fever (>38C), urgency, frequency, dysuria, or suprapubic tenderness *and* patient has a positive urine culture, that is, $\geq 10^5$ microorganisms per cc of urine with no more than 2 species of microorganisms.
2. Patient has at least 2 of the following signs or symptoms with no other recognised cause: fever (>38°C), urgency, frequency, dysuria, or suprapubic tenderness and at least 1 of the following
    a. positive dipstick for leukocyte esterase and/ or nitrate
    b. pyuria (urine specimen with ≥10 white blood cell [WBC]/mm3 or ≥3 WBC/high- power field of unspun urine)
    c. organisms seen on Gram's stain of unspun urine
    d. at least 2 urine cultures with repeated isolation of the same uropathogen (gram- negative bacteria or *Staphylococcus saprophyticus*) with $\geq 10^2$ colonies/mL in non-voided specimens
    e. $\leq 10^5$ colonies/mL of a single uropathogen (gram-negative bacteria or *S saprophyticus*) in a patient being treated with an effective antimicrobial agent for a urinary tract infection
    f. physician diagnosis of a urinary tract infection
    g. physician institutes appropriate therapy for a urinary tract infection.
3. Patient ≤1 year of age has at least *1* of the following signs or symptoms with no other recognised cause: fever (>38°C rectal), hypothermia and at least *1* of the following:
    a. positive dipstick for leukocyte esterase and/ or nitrate

b. pyuria (urine specimen with ≥10 WBC/mm3 or ≥3 WBC/high-power field of unspun urine)
c. organisms seen on Gram's stain of unspun urine
d. at least 2 urine cultures with repeated isolation of the same uropathogen (gram- negative bacteria or *S saprophyticus*) with $\geq 10^2$ colonies/mL in non-voided specimens
e. ≤105 colonies/mL of a single uropathogen (gram-negative bacteria or *S saprophyticus*) in a patient being treated with an effective antimicrobial agent for a urinary tract infection
f. physician diagnosis of a urinary tract infection
g. physician institutes appropriate therapy for a urinary tract infection

<u>Primary bloodstream infection (PBI)</u>

PBI criteria 1 and 2 may be used for patients of any age, including patients ≤1 year of age.

PBI must meet at least *1* of the following criteria:

1. Patient has a recognised pathogen cultured from 1 or more blood cultures *and* organism cultured from blood is not related to an infection at another site.
2. Patient has at least *1* of the following signs or symptoms: fever (>38°C), chills, or hypotension *and* signs and symptoms and positive laboratory results are *not* related to an infection at another site *and* common skin contaminant (ie, diphtheroids [*Corynebacterium* spp], *Bacillus* [not B anthracis] spp, *Propionibacterium* spp, coagulase-negative staphylococci [including *S*

epidermidis], viridans group streptococci, *Aerococcus* spp, *Micrococcus* spp) is cultured from 2 or more blood cultures drawn on separate occasions.

3. Patient ≤1 year of age has at least *1* of the following signs or symptoms: fever (>38°C, rectal), hypothermia (<37°C, rectal), apnea, or bradycardia *and* signs and symptoms and positive laboratory results are *not* related to an infection at another site *and* common skin contaminant (ie, diphtheroids [*Corynebacterium* spp], *Bacillus* [not *B anthracis*] spp, *Propionibacterium* spp, coagulase-negative staphylococci [including *S epidermidis*], viridans group streptococci, *Aerococcus* spp, *Micrococcus* spp) is cultured from 2 or more blood cultures drawn on separate occasions.

Depth of burn injury [41]:

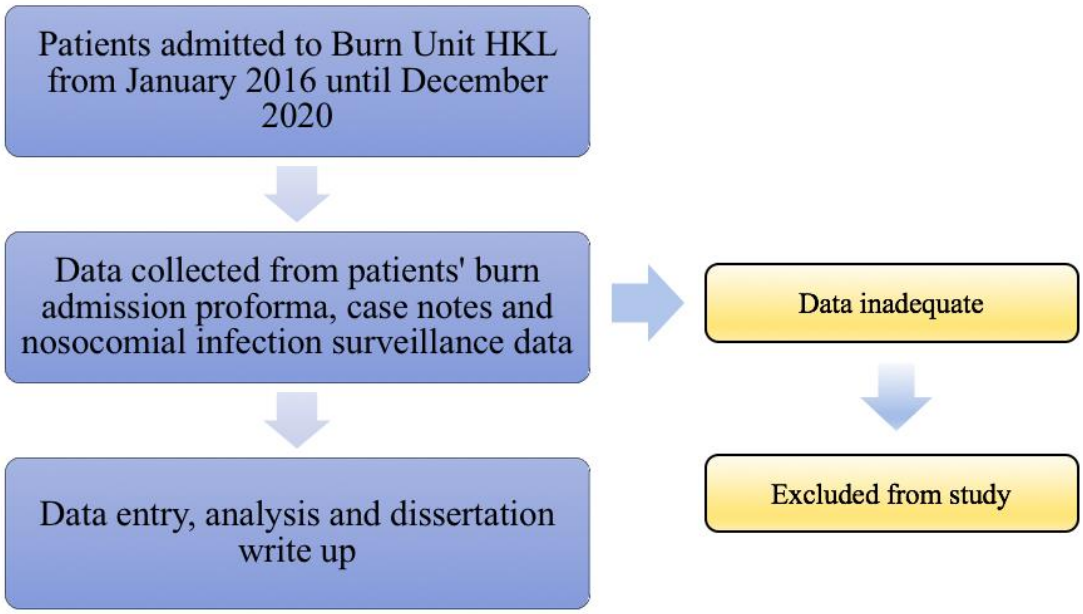
Superficial burn	Burn injury only involving the epidermis.
Superficial dermal thickness burn	Burn injury extending into the papillary dermis.
Deep dermal thickness burn	Burn injury extending into the reticular dermis.
Full thickness burn	Burn injury involving the entire dermis and extending into the subcutaneous tissue.

3.9 Data collection method

Patient's details were collected from the admissions book, burn admission proforma and nosocomial infection surveillance data located at the Burn Unit. Patient's hospital case notes were then traced from the Medical Record Unit of Kuala Lumpur Hospital. All data relevant to the study were filled into the data collection sheet and

entered into Statistical Package for Social Science (SPSS) for analysis. All data was archived for reasons of scientific integrity for 5 years after completion of the project.

3.10 Study flow chart



3.11 Statistical data analysis

Data was entered and analysed using Statistical Package for Social Science (SPSS) version 27. Descriptive analysis was used to summarise the socio-demographic characteristics of subjects. Numerical data was presented as mean (SD) or median (IQR) based on their normality distribution. Categorical data was presented as frequency (percentage) for all the objectives. To determine the prevalence of health care associated infections at the Hospital Kuala Lumpur Burn Unit, we obtained the proportion of the patients who developed HAIs divided by all the patients with acute burn injuries admitted to the burn unit during the study period.

To determine the most common causative organisms during the early and late stages of infection, we attained the proportion of each causative organism divided by all the causative organisms identified.

To assess for the risk factors associated with the development of health care-associated infection, we used chi-square test at bivariate to assess for factors that could have an independent association with HAIs. Variables with a P-value < 0.2 were considered for the multivariate model. At multivariate analysis, first the assumption of no collinearity was assessed and there was collinearity between inhalation burns, ventilation and indwelling catheter. Therefore, ventilation and indwelling catheter were dropped and inhalation burns considered for analysis. Variables from bivariate were run in the logistic regression model using the backward stepwise method and variables with P-values < 0.05 were retained in the model and assessed for interaction using the chunk test. From the backward stepwise analysis, variables that were dropped were assessed for confounding. Variables that had a more than 10% difference between the crude and adjusted odds ratios were considered to be confounders. All variables that had P-values less than 0.05 were considered to be risk factors for HAIs.

3.12 Benefit of this study

This study aims to address the paucity of local data on infections in Burn Units. The last known study to be conducted on burns at the Hospital Kuala Lumpur was in 1987 whilst under the care of the Orthopaedics and Traumatology Department. With the creation of a specialised Burn Unit, staffed by trained personnel with a special interest in burn management, this study will report data of burn care under the Plastics and Reconstructive Surgery Department. Infection is one indicator of

outcome in the field of quality assurance in burn management. Microbiological surveillance helps provide knowledge of the responsible bacterial flora of health care-associated infections in the burn patient, its prevalence, and bacterial resistance. It is also of crucial importance for fast and reliable therapeutic decisions. Measures to prevent and treat infections are essential for the survival of patients with extensive burns and infection is correlated to mortality. Careful surveillance of infection along with good isolation techniques and procedure routines can keep antimicrobial resistance rates and infection rates low in infection-prone burn patients.

3.13 Gantt chart and milestone

	2021								
	Mar	Apr	May	Jun	Jul	Aug	Sep	Oct	Nov
Proposal presentation									
Proposal submission and ethical approval									
Data collection									
Data analysis									
Dissertation preparation and write up									
Presentation and publication									

3.14 Ethical consideration

This study was conducted in compliance with the ethical principles outlined in the Declaration of Helsinki and Malaysian Good Clinical Practice Guidelines. Ethical approval from Medical Research and Ethics Committee (MREC) (approval code: NMRR-21-935-59913) and The Human Research Ethics Committee of USM

(JEPeM-USM) (approval code: USM/JEPeM/21060425) was obtained prior to the start of any study related activities.

3.14.1 Privacy and confidentiality

All forms were anonymous, and data was entered into SPSS software. Only research team members were allowed to access the data. Data was presented as grouped data and could not identify the participants individually.

3.14.2 Honorarium and incentives

This is a self-sponsored study.

3.14.3 Risk

There was no risk to the health of participants applicable for this research.

3.14.4 Archives of study data

The storage and archival of study data and records of hardcopy data collection forms were kept in the office of Plastic and Reconstructive Surgery Department, Hospital Kuala Lumpur (HKL). Database was kept for the whole duration of the study and five years from the date of final publication. After this period, both hardcopies and softcopies of research data will be destroyed in accordance with the Universiti Sains Malaysia research governance procedures.

3.14.5 Publication

After the manuscript is submitted as thesis, investigators will attempt to submit for publication in local or international journal. No personal information of subjects will be published. Prior to publication, permission from the Director General of Health, Malaysia will be obtained.

3.15 Conflict of interest statement

The authors declare that there is no conflict of interest.