CATHETER-RELATED BLOOD STREAM INFECTIONS CAUSED BY PATHOGENIC BACTERIA IN HOSPITAL QUEEN ELIZABETH KOTA KINABALU FROM 2009 – 2015

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FACULTY OF MEDICINE AND HEALTH SCIENCES
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2018

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Jaistin bin Tamin

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ABSTRACT

Blood stream infections (BSI) are the most common hospital-acquired infections. Rapid diagnosis and timely intervention are the key factors in preventing morbidity and mortality. With a mortality rate of 12% – 25%, CRBSI is the most serious nosocomial infections. This study investigated the antibiotic susceptibility patterns, the epidemiology of BSI, the frequency of BSI pathogens and multi-drug resistant isolates, the role of ethnic variation and the prevalence of BSI. Hospital laboratory records on BSI cases of patients admitted into the intensive care unit of Hospital Queen Elizabeth and Hospital Queen Elizabeth II from 2009 to 2015 were examined and analysed. Within this period, there were 11,420 BSI cases of which, a total of 1699 or 14.9% were CRBSI. Kadazan-Dusun (26.9%, 457) was the most common ethnic group encountered in the CRBSI cases, followed by Chinese (16.1%, 274) and Bajau (15.2%, 258). The frequency of CRBSI occurs mostly for in patients in the age group of 51 - 60 which was 22.4% (380), and the age groups of 41 – 50 (16.6%, 282) and 61 – 70 (17.6%, 299). The top five organisms were Coagulase Negative *Staphylococcus* (282, 17.2%), *Staphylococcus aureus* (177, 10.8%), *Pseudomonas aeruginosa* (124, 7.6%), *Burkholderiapseudomallei* (111, 6.8%) and *Klebsiellapneumoniae*(111, 6.8%). A significant uptrend in antibiotic resistant patterns were observed during the study period especially for *Acinetobacterbaumanii* which was gaining resistance to most of the antibiotics although still susceptible to Polymxin B. *Klebsiellapneumoniae* also noted with increasing resistance to cefoperazone (96.2%), cefuroxime (94.4%), ciprofloxacin (57.1%) and amoxicillin-clavulanic acid (87.5%). In conclusion, there is a need to continually review the antibiograms pattern periodically to formulate the best empiric antimicrobial treatment. Since there is no known study was done in Sabah, it is expected that this study will provide a microbiological basis that may be relevant to BSI in Sabah, and these informations will help clinicians in initiating the empirical antibiotic therapy based on local data and thus preventing the emergence of multi-drugs resistant microorganisms. The study will also improve our understanding on the importance of CRBSI in the Sabah hospitals.

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ABSTRAK

KAJIAN MENGENAI CORAK SENSITIVITI ANTIBIOTIK DI DALAM JANGKITAN ALIRAN DARAH YANG BERKAITAN KATETER DI HOSPITAL QUEEN ELIZABETH SABAH DARI TAHUN 2009 - 2015

Jangkitan aliran darah (BSI) adalah jangkitan yang paling kerap diperolehi di hospital. Pendiagnosan yang cepat dan intervensi yang tepa tmerupakan kunci utama dalam mengelakkan morbidity dan mortaliti. Kadar penyebab kematian sebanyak 12 – 25% menjadikan CRBSI jangkitan nosocomial yang paling merbahaya. Kajian ini menyiasat corak sensitivity antibiotik, epidemiologi BSI, kekerapan patogen BSI yang rentan terhadap kebanyakan antibiotik, mengkaji perkaitan antara variasi etnik dan kekerapan BSI, dan menyelidik corak kerentanan antibiotik. Kajian ini melibatkan data daripada kes-kes BSI dari pesakit yang dimasukkan ke dalam wad rawatan rapi di Hospital Queen Elizabeth dan Hospital Queen Elizabeth II dalam tempoh masa 7 tahun dari tahun 2009 sehingga tahun 2015. Sebanyak 11,420 kes BSI telah dikesan dan daripada jumlah ini, sebanyak 1699 atau 14.9% adalah CRBSI. Kadazan-Dusun (26.9%, 457) merupakan etnik yang paling kerap ditemui dalam kes CRBSI diikuti kaum Cina (16.1%, 274) dan Bajau (15.2%, 258). Kekerapan CRBSI didapati berlaku dalam kumpulan umur 51 - 60 iaitu 22.4% (380), kumpulan umur 41 – 50 (16.6%, 282) dan 61 – 70 (17.6%, 299). Lima organisma utama yang didapati menyebabkan CRBSI ialah Coagulase Negative Staphylococcus (282, 17.2%), Staphylococcus aureus (177, 10.8%), Pseudomonas aeruginosa (124, 7.6%), Burkholderia pseudomallei (111, 6.8%) dan Klebsiella pneumonia (111, 6.8%). Corak kerentanan antibiotik yang menunjukan peningkatan dapat dilihat di dalam sepanjang tempoh kajian terutamanya bagi Acinetobacter baumanii yang menunjukkan peningkatan kerentanan terhadap kebanyakan antibiotik walaupun buat masa ini masih sensitive kepada Polymyxin B. Klebsiella pneumoniae yang menunjukkan peningkatan kerentanan terhadap cefoperazone (96.2%), cefuroxime (94.4%), ciprofloxacin (57.1%) dan amoxicillin-clavulanic acid (87.5%). Memandangkan tiada kajian seperti ini pernah dibuat di Sabah, maka adalah diharapkan kajian ini dapat memberikan maklumat yang akan menjadi asas mikrobiologikal yang relevan kepada BSI di Sabah dan dengan ini akan membantu para ahli perubatan klinikal dalam memberikan rawatan empirikal yang berdasarkan kepada data tempatan untuk mengelakkan kemunculan bakteria rentan antibiotik. Kajian ini juga akan meningkatkan pengetahuan dan kefahaman mengenai kepentingan CRBSI di hospital-hospital di negeri Sabah.

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LIST OF ABBREVIATIONS

CRBSI - Catheter-Related Blood Stream Infection

BSI - Blood stream infections

SIRS - Systemic Inflammatory Response Syndrome

MODS - Multiple Organ Dysfunction Syndrome

CDC - Centers for Disease Control and Prevention

NNIS - National Nosocomial Infection Surveillance

CLABSI - Central Line-Associated Blood Stream Infections

ICU - Intensive Care Unit

CVC - Central venous catheter

HAI - Hospital-Acquired Infections

CoNS - Coagulase Negative Staphylococcus

MRSA - Methicillin-Resistant *Staphyloccocus aureus*

MSSA - Methicillin-Sensitive *Staphyloccocus aureus*

IDSA - Infectious Diseases Society of America

DTP - Differential time to positivity

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CHAPTER 1

INTRODUCTION

1.1 Background

The presence of viable bacteria in the blood constitutes bacteremia. Bacteremia reflects active and possibly spreading of infection in the tissue. According to Illyasu *et al* (2016), a case of primary bacteraemia was defined based on documentation of isolated bacteria from blood without any identified focus of infection. The prognosis of such bacteremia or septicemia may well depend on its prompt recognition by microbiological methods. Blood stream infections (BSI) are the most common hospital acquired or nosocomial infections. BSI may cause systemic inflammatory response syndrome (SIRS) and multiple organ dysfunction syndrome (MODS). Prompt diagnosis and early intervention are key factors in preventing morbidity and mortality from BSI. Rates of central venous catheter associated bacteremia has been reported by the Centers for Disease Control and Prevention (CDC's) Nosocomial Infection Surveillance (NNIS) system since 1970. As early as 1977, Maki suggested that more than 25,000 patients developed device-related bacteremia in the United States each year (Maki, 1977). CDC has estimated that approximately 80,000 central line-associated blood stream infections (CLABSIs) occur in intensive care units (ICUs) each year (Edwards *et al*, 2007). Menon*,* Mustafa and Sannasey (2002) reported in one prospective study in the ICU patients in Sabah that 21.4% of the nosocomial infections were vascular catheters related.

Intravascular devices are essential in modern clinical practice especially in intensive care units (ICUs). Central venous catheters (CVCs) are commonly inserted in critically ill patients. Although such catheters provide necessary vascular access, their use puts patients at risk for local and systemic infectious complications,

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including local site infection, CRBSI, septic thrombophlebitis, endocarditis, and other metastatic infections (e.g., lung abscess, brain abscess, osteomyelitis, etc.).

Catheter-related bloodstream infection (CRBSI) was defined as bacteremia in the setting of intravascular catheter infection with no other apparent source (Illyasu *et al*, 2016). Approximately 90% of the CRBSI occur with CVCs (O' Grady *et al*, 2002). The risk of infection depends on the type of device, the site of insertion, the underlying conditions and the appropriate prevention measures taken during catheter insertion. Management of catheter-related bloodstream infection involves decision on catheter removal, antimicrobial catheter lock solution and the type and duration of systemic antimicrobial therapy. Most CRBSIs emanate from the insertion site and skin is a prominent source of microbes causing bloodstream infection (Mermel *et al*, 2009). Catheter-Related Blood Stream Infections (CRBSI) are some of the most significant of all hospital-acquired infections (HAIs), both clinically and financially. In the United States alone, about 250,000 central venous CRBSIs occur every year and they are among the most dangerous Hospital-Acquired Infections, with an attributable mortality rate of 12 – 25% (Mermel *et al*, 2009).

There were 4 major sources of infection - colonization from skin, intraluminal or hub contamination, secondary seeding from a bloodstream infection, and rarely contamination of the infusate. The incidence of CRBSI varies considerably by type of catheter, frequency of catheter manipulation, and patient-related factors, for examples underlying disease and acuity of illness (Mermel *et al*, 2009). Mermel *et al* study also found that the peripheral venous catheters are the devices most frequently used for vascular access. Although the incidence of local or bloodstream infections (BSIs) associated with peripheral venous catheters is usually low, serious infectious complications produce considerable annual morbidity caused by the frequency of usage of such catheters. However, the majority of serious catheter-related infections are associated with central venous catheters (CVCs), especially those that are placed in patients in ICUs. In the ICU setting, the incidence of infection is often higher than in the less acute in-patient or ambulatory setting. Furthermore, central venous access might be needed for extended periods of time in the ICU. Therefore, patients can be colonized with hospital-acquired organisms; and the catheter can be manipulated multiple times per day for the administration of fluids, drugs, and blood products.

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Moreover, some catheters need to be inserted in urgent situations, during which optimal attention to aseptic technique might not be feasible. As mentioned in the *Guidelines for the Prevention of Intravascular Catheter-Related Infections* (2002), certain catheters (e.g., pulmonary artery catheters and peripheral arterial catheters) can be accessed multiple times per day for hemodynamic measurements or to obtain samples for laboratory analysis, augmenting the potential for contamination and subsequent clinical infection. The extent of the potential for CVCs to cause morbidity and mortality resulting from infectious complications has been estimated in several studies. In a study by Mermel (2000) in the United States, 15 million CVC days (i.e., the total number of days of exposure to CVCs by all patients in the selected population during the selected time period) occur in ICUs each year. If the average rate of CVC-associated BSIs is 5.3 per 1,000 catheter days in the ICU, approximately 80,000 CVC-associated BSIs occur in ICUs each year in the United States (CDC, 1998). The attributable mortality for these BSIs has ranged from no increase in mortality in studies that controlled for severity of illness (Digiovine *et al*, 1999; Rello *et al*, 2000; Soufir *et al*, 1999), to 35% increase in mortality in prospective studies that did not use this control. (Collignon *et al*, 1994; Pittet, Tarara and Wenzel, 1994). Thus, the attributable mortality remains unclear.

Although intravascular catheters represent an essential part in managing critical and chronic ill patients, it's usage is often complicated by serious infections, mostly CRBSIs, which are associated with increased morbidity, duration of hospitalisation, and additional medical costs (Dimick *et al*, 2001; Mermel, 2000). However, as mentioned in The Joint Commission 2009 National Patient Safety Goals Hospital Program (2009), the majority of CRBSIs are associated with central venous catheters (CVCs), and in prospective studies the relative risk for CRBSI is up to 64 times greater with CVCs than with peripheral venous catheters (Hugonnet *et al* ,2003; Lorente *et al*, 2005; NNIS, 2004).

Different measures have been implemented to reduce the risk for CRBSI, including use of maximal barrier precautions during catheter insertion, effective cutaneous antisepsis, and preventive strategies based on inhibiting microorganisms originating from the skin or catheter hub from adhering to the catheter. Institution

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of continuous quality improvement programs, education and training of health care workers, and adherence to standardized protocols for insertion and maintenance of intravascular catheters significantly reduced the incidence of catheter-related infections and represent the most important preventive measures (Gowardman *et al*, 1998; Safdar *et al*, 2004). In the present review the new technologies for prevention of infections directed at CVCs, which have been shown to reduce the risk of CRBSI, including catheters and dressings impregnated with antiseptics or antibiotics, new hub models, and antibiotic lock solutions.

For short-term CVCs (i.e. those in place <10 days), which are most commonly colonized by cutaneous organisms along the external surface of the catheter, the most important preventive systems are those that decrease the extraluminal contamination. In contrast, with long-term CVCs (i.e. those in place >10 days), in which endoluminal spread from the hub appears to be the primary mechanism of infection, technologies that reduce endoluminal colonization in addition to extraluminal invasion of the catheter should provide additional protection against CRBSI. (Gowardman *et al*, 1998; Safdar *et al* 2004; Sadoyama *et al*, 2003).

Although many organisms can cause BSI, community-acquired bacteremia may be due to *pneumococcal* infections, bacterial meningitis, typhoid fever, wound infections caused by haemolytic *Streptococci,* and *Staphylococcus aureus. Staphylococcus* continues to predominate as the most frequent encountered pathogens in device-related infections. Other commonly encountered isolates in catheter associated infection caused by gram negative bacilli (Weinstein *et al*, 1997). The past decade has witnessed an increasing occurrence of CLABSIs caused by multiple drug resistant gram negative bacilli, most notably *Acinetobacter spp* (Hugonnet *et al*, (2003). Statistically, a number of studies in the United States reported coagulase negative staphylococci (CoNS) as the most common organism (Lorente et al, 2005; Gowardman *et al*, 1998; Weinstein *et al*, 1997; Hugonnet *et al*, 2003). Mermel *at al* (2001) has also reported that the most common bacteria-causing CRBSI associated with percutaneously inserted catheters are coagulase-negative staphylococci, *S. aureus*, *Candida* species, and enteric gram-negative bacilli (Nakamura *et al*, 2015). In 2010, Sang Taek Heo and his team reported the first case

of catheter-related bloodstream infection caused by *Nocardia farcinica* (Sang *et al*, 2010).

In a survey by Richard *et al* (1999) on 112 medical ICUs in the United States, they found that the most common causatives of CRBSIs were CoNS, mostly *Staphylococcus epidermidis* (36%), Enterococci (16%), Gram-negative aerobic bacilli (16%), (*Pseudomonas aeruginosa, Klebsiella pneumoniae, Escherichia coli,* etc.), *Staphylococcus aureus* (13%) Candida species (11%) and other organisms (8%). In one of the studies, O'Grady *et al* (2002) found out that the common pathogens were CoNS 37%, *Staphylococcus aureus* 13%, *Enterococcus* sp 13%, *Enterobacter spp* 5%, *Pseudomonas aeruginosa* 4%, *Klebsiella pneumoniae* 3%, *Escherichia coli* 2% and *Candida species* 8%. However, a study done in Hospital Sultanah Aminah, Johor Baru (HSA-JB) Malaysia in 2005 by Tan *et al* (2007), presented a completely different scenario. In this study, the most common pathogen encountered was the Gram negative bacteria which constitutes 80.6% of the pathogens (Klebsiella *pneumoniae* 38.9%, *Pseudomonas aeruginosa* 19.4%, *Acinetobacter baumanii* 13.9% *Enterobacter* sp 8.3%), 19.4% Gram positive bacteria (MRSA 13.9%, MSSA 2.8%, CoNS (2.8%). Similar findings was encountered in a CRBSI study done in a haemodialysis settings in Universiti Kebangsaan Malaysia Medical Centre (UKMMC), Bangi, Malaysia by Abdul Gafor *et al* (2014). In that study, the most common encountered organisms were the Gram negative (44.4%), followed by Gram positive (38.9%) and the remaining 16.7% were polymicrobial isolates.

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The laboratory results of blood cultures are crucial in determining or establishing the case of bacteremia. However, there are possibilities of false negative results. Since the standard incubation periods of a blood culture is 5 days, there are possibilities of undetectable bacteria growth within that period such as in a case of slow growing bacteria of HACEK group. HACEK group comprises of fastidious, slow growing bacteria of *Haemophilus, Aggregatibacter (*formerly *Actinobacillus), Cardiobacterium, Eikenella,* and *Kingella*. False positive blood culture results could be caused by contamination during sampling, mostly by the skin floras such as *Staphylococcus epidermidis* or *Bacillus* sp. Improper cleaning and skin disinfection may introduce the bacteria into the possibly sterile blood sample. Mixed positive