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Prospective surveillance of nosocomial device-associated bacteremia in three adult intensive units in Malaysia

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Abstract. Nosocomial blood stream infection (or nosocomial bacteremia) is a common problem in hospitals worldwide, including Malaysia. A three-year prospective cohort study (October 2003–March 2007) of the incidences, risk factors, and patterns of the microorganisms causing bacteremia was conducted using a validated surveillance form in three intensive care units (ICUs) in Malaysia. Center for Disease Control criteria were used to diagnose bacteremia. Patients were monitored from admission until the end point of study, which was the first detection of bacteremia in the blood in each patient. The frequency of occurrence of bacteremia with clinical symptoms was 10.7% (n = 23). Bacteremia was observed to occur within a mean length of stay of 10 days in ICU. The rate of device-related infection was 10.4% per device utilization days with a device utilization rate of 95.9%/1000 patient days. The total number of patient days was 2309 and the period of device utilization was 2211 days. The common bacteria detected were extended-spectrum beta-lactamases (ESBLs) *Klebsiella pneumoniae* (n = 6); *Pseudomonas aeruginosa* (n = 6); *Acinetobacter* species (n = 5); Methicillin-resistant *Staphylococcus aureus* (MRSA)(n = 3); and (non- ESBL) *Klebsiella pneumoniae* (n = 2). Multivariable analysis using Cox Proportional Hazard Model showed that the predictors for developing bacteremia were cancer, MRSA carriage, duration of central venous catheter (CVC) infusion, frequency change of CVC, and the administration of hydrocortisone drugs. These results indicate that a combination of nursing and medical interventions as well as patients' severity of illness could lead to bacteremia in ICU. Strategic implementation of quality assurance measures in ICUs could help to control this problem.

INTRODUCTION

Nosocomial blood stream infection (or nosocomial bacteremia) is a common problem in hospitals worldwide, including Malaysia. Nosocomial bacteremia with sepsis is potentially life threatening among immunocompromised patients in intensive care units (ICUs) (Rozaidi *et al.*, 2000; Hughes *et al.*, 2005; Katherason *et al.*, 2008), and it increases the length of stay in the ICU. An estimated 200 000 to 300 000 cases occur each year, with mortality rates varying from 17.5% to 50% (Reimer *et al.*, 1997). Furthermore, respiratory, urinary tract, and gastrointestinal infections

potentially can contribute to blood stream infection (Reimer *et al*., 1997; Weinstein *et al*., 1997).

A number of risk factors associated with nosocomial infections (NI) and bacteremia are mentioned in literature. The most typical risk factors suggested for review included severity of illness, reduced immune function of a patient, use of intravascular catheters (e.g., central venous catheter, CVC), duration of usage of intravascular catheters, management of intravascular catheter sites, increased length of stay in the ICU, and use of antibiotics (Reimer *et al*., 1997; Weinstein *et al*., 1997; Magadia *et al*., 2001; Crnich & Maki, 2002). Furthermore, lack of infection control practices, such as hand washing, gloving techniques, and medical-surgical asepsis are additional aggravating factors.

Accurate population-based estimates of incidences and contributing factors of NI to date, and acceptable data on the contributing factors and risk prediction of nosocomial bacteremia in Malaysia are limited. The few local studies conducted in hospitals in Malaysia reported data on point prevalence, bacterial resistance patterns and antibiotic therapy (Rozaidi *et al*., 2000; Hughes *et al*., 2005). A high incidence of bacteremia was reported among patients treated with central venous lines and those with indwelling intravascular catheters in Rosaidi *et al*. study (1988–1999) (prevalence-23%) and Katherason *et al*. study (2003–2006) (incidence-29.3%) in Malaysia. However, these studies (Rozaidi *et al*., 2000; Hughes *et al*., 2005) differed in their sampling methods; inclusion and exclusion criteria; details about predictors of bacteremia; definition of NI; layout of units and suitable facilities; and adequacy of training of staff with varying degrees of experience (Rozaidi *et al*., 2000; Hughes *et al*., 2005; Katherason *et al*., 2008). The observed differences in contributing factors and rates in Malaysia likely depended on the individual hospitals and their own practices, policies, patient-to-staff ratios, and unique microbiological flora. These factors contribute to the existing gap in our knowledge of the epidemiology of ICU NIs in Malaysia. Empirical evidence also shows diverse patterns of infection control practices among Malaysian staff working in ICUs (Tan, 1998). These mentioned diverse practices in different ICUs need to be standardized.

Therefore, the goal of this study was to examine the magnitude and occurrence of device-related ICU-acquired nosocomial bacteremia and its specific risk factors in Malaysia. The type of bacterial patterns and time taken for occurrence of bacteremia since admission into ICU also were recorded. Our results will help generate awareness and development of good prevention strategies to decrease nosocomial bacteremia in the three ICUs studied.

MATERIALS AND METHODS

Study design

A prospective cohort observational study of infections that occurred in the ICU was conducted using a validated surveillance form in three adult ICUs in Malaysia from October 2003 to March 2007.

Setting

The ICUs studied were part of the Hospital Universiti Sains Malaysia, Hospital Ipoh, and Hospital Terengganu.

The Hospital Universiti Sains Malaysia has a 12-bed general ICU. The average length of stay in ICU varied from 10.9 to 27.6 days, and the bed occupancy rate was 42.4% to 73.7% during the study period (Laporan Hospital USM, 2006).

Hospital Ipoh has an ICU with a capacity of 16 beds. The average length of stay in ICU varied from 5.37 to 3.94 days and the bed occupancy rate was 57.24% to 69.4% during the study period (Laporan Hospital Ipoh, 2005).

The ICU in the Hospital Kuala Terengganu also has 16 beds. The average length of stay in ICU varied from 5 to 3 days, and the bed occupancy rate was 75% in the hospital during the study period.

Subjects and sample size

We reviewed 864 patients upon admission to the three ICUs as a cohort group, but only 215 patients without infection at the time of admission were included in the study. Because the focus of this study was on infection that developed in the ICU, patients who developed infection in wards before being admitted to the ICU were excluded from the study. Patients who developed infection within 48 hours of admission to the ICU were also excluded because the infection must have been acquired outside of the ICU. The multiracial subjects included in the study were 18 years old and more, had intravascular devices (CVC, intra-arterial catheter, and peripheral venous catheter) inserted within 48 hours, and had no clinical manifestation of NI upon admission to the ICU. These patients were admitted from the operation theatres, emergency rooms, or other wards.

Definitions

In the present study, bacteremia refers to the presence of bacteria in the blood. Septicaemia refers to blood infection combined with clinical signs and symptoms along with a positive culture among critically ill patients in ICUs. Sepsis refers to severe systemic infection leading to organ dysfunction and septic shock (CDC, 1994).

Criteria for diagnosis

Bacteremia was diagnosed using the Center for Disease Control and Prevention (CDC, 1994) criteria and the National Nosocomial Infection Surveillance System (NNIS, 2004) definitions. In this study, bacteremia was confirmed by positive microbiology culture results of blood samples and associated clinical manifestations.

Catheter-related blood stream infection (BSI) was considered to be associated with a central line if the line was inserted 48 hours prior to the development of BSI. If the time interval between onset of BSI and the device used was > 48 hours, then the NI was considered to be related to CVC, provided there were no other sites of infection in the body (CDC, 1994). Bacteremia was confirmed if there was at least one positive blood culture obtained from the peripheral vein, clinical manifestations of NI were evident, and there was no apparent source for BSI.

Instrument and validation

A validated surveillance form was developed and used for data collection.

This instrument was used to measure the incidence and risk factors of bacteremia in the three ICUs. The form addressed demographic data; diagnosis upon admission, history of illness, severity of illness, nutritional status, medications, antibiotics, laboratory blood results, coagulation profile, liver function tests, clinical evidence of infections, and results of microbiology, laboratory, and X-ray investigations. The severity of illness was measured using the APACHE III Score (Acute Physiology and Chronic Health Evaluation). The age, gender, cause of admission, severity of underlying diseases, and organ dysfunction upon admission was assessed using APACHE III. The intensity of treatment was recorded using the Therapeutic Intervention Scoring System (TISS). Physiological condition was assessed using the Simplified Acute Physiology Score (SAPS II).

Procedure

The validated form was used for prospective on-going data collection from case records, laboratory reports, results of clinical findings, and direct observation by the researchers. The patients studied were monitored daily from the time of admission until discharge from the ICU for early clinical signs of blood infection and for the first positive culture of bacteremia. The end point of study was the first detection of bacteremia in the blood in each patient. The patients were followed-up for 48 hours post ICU discharge to include NI manifestations that occurred in the wards.

Ethical approval

The Human Ethics and Research Committee, Universiti Sains Malaysia,

approved the study in October, 2003. Permission was also obtained from the three hospitals. Informed consent was requested and obtained from the patients' close relatives (husband, wife, children, or parents).

Statistical analysis

The results were collated and analyzed using SPSS version 12.0.1. Means and standard deviations (SD) were calculated for numerical variables. Frequency and percentages were calculated for categorical variables. The NI incidence-density rate was calculated as the number of NI cases per 1000 patient-days. The BSI rate was calculated as the number of device-associated bacteremia cases per 1000 "patients on intravascular devices." The device utilization rate (DUR) is the proportion of patient days for which a certain device is used. The DUR reflects the number of devices used and is a reflection of patient severity of illness. The DUR was calculated as the number of device days per 1000 patient days.

Simple Cox regression and multivariable Cox proportional hazard regression model analyses were performed to detect the risk factors for BSI. The results are expressed in 95% confidence intervals (*CI*), Hazard Risk (*HR*), Wald stats and *P* value.

RESULTS

Characteristics of subjects

Two hundred and fifteen patients with no signs of infection within 48 hours of admission were studied. The mean (SD) age of patients was 42 (17.05) years. Most of the subjects were male (72.6%; n = 156). The study population consisted of Malays (57.2%) followed by Chinese (19.5%), Indian (19.1%), and other ethnicities (4.2%).

The mean (SD) severity scores upon admission were SAPS II score of 45.5 (16.87), TISS score of 50.1 (11.62), and APACHE III score of 87.7 (30.15). The mean (SD) length of stay (days) in the ICU was 11 (6.51). The average (SD) duration of observation (days) was 11 (5.86).

Epidemiology

The frequency of occurrence of bacteremia with clinical symptoms was 10.7% (n=23). Bacteremia was observed within a mean (SD) duration stay of 10.5 (5.00) days. The rate of device-related infection was 10.4% per device utilization day. The device utilization rate was 95.9%/1000 patient days. The total number of patient days was 2309 and the total period of device utilization was 2211 days.

Microbiology

The major groups of bacteria detected were extended-spectrum beta-lactamases (ESBLs): *Klebsiella pneumoniae* (n = 6); non-ESBL *K. pneumoniae* (n = 2). *Pseudomonas aeruginosa* (n = 6); *Acinetobacter* spp (n = 5); Methicillin-resistant *Staphylococcus aureus* (MRSA)(n = 3); and The other organisms were Methicillin-resistant *Staphylococcus epidermis* (MRSE), enterococccus species, and enterobacter species.

The drug sensitivity patterns showed that the ESBL *K. pneumoniae* were resistant to cephalosporins, amikacin, ampicillin, imipenum, piperacillin, and cotrimoxazole where as sensitive to cefuroxime (n = 1), cefotaxime (n = 1), and ceftazidime (n = 2). *Pseudomonas aeruginosa* was sensitive to all of the antibiotics tested.

MRSA was resistant to ampicillin, ceftazidime, cloxacillin, cotriamazole, erythromycin, gentamycin, and penicillin-G and was sensitive to fucidic acid, rifampicin, and vancomycin. *Acinetobacter* spp was resistant to amikacin, ampicillin, cefoperazone sodium, cefotaxime, ceftazidime, cefuroxime, ciproflocaxin, cotrimazole, and imipenum and was sensitive to gentamycin and netilmycin. MRSE was resistant to cotrimoxazole, erythromycin, and fucidic acid and was sensitive to gentamycin, rifampicin, and vancomycin.

Predictors

The intrinsic predictor identified for developing bacteremia was cancer. The extrinsic predictors identified were MRSA *carriage* (in the axilla, perineum, groin or throat), duration of central venous catheter (CVC) infusion, frequency of change of CVC, and the administration of hydrocortisone drugs. Table 1 lists the potential risk factors.

DISCUSSION

This study has observed and analyzed the incidence and predictors of bacteremia in the ICUs of the three hospitals in Malaysia. An incidence of 29.3% was observed in this study. When compared with the studies available from the region, the incidence was found to be higher than that reported by Agodi *et al.* (2009) (17.1%) and lower

Table 1. Potential Predictors of Bacteremia using Simple Cox Regression: Socio-demographic characteristics and Length of Stay (n = 215)

Variable	Crude Hazard Ratio (95% *CI*)	Wald Stat (*df*)	*P* value
Age (years)	1.02 (1.00‘,1.05)	2.50 (1)	0.114
Race			
Non-Malays	1.00	–	–
Malays	2.84 (1.05, 7.65)	4.25 (1)	0.039
Sex			
Male	1.00	–	–
Female	2.12 (0.93, 4.86)	3.16 (1)	0.075
Type of cases			
Medical	2.84 (1.24, 6.51)	6.09 (1)	0.014
Length of Stay in ICU	1.07 (1.02, 1.12)	9.22 (1)	0.002
APACHE III upon admission	1.02 (1.00, 1.03)	4.11 (1)	0.043
MRSA			
Perineum	9.61 (2.76, 33.54)	12.60 (1)	0.001
Axilla			
Throat			
Duration of Endotracheal tube	1.08 (1.05, 1.13)	18.35 (1)	0.001
Oral toilet (number of times per day)	1.28 (1.02, 1.61)	4.49 (1)	0.034
Duration of Mechanical Ventilation	1.08 (1.05, 1.13)	18.47 (1)	0.001
Frequency change ETT			
No Change	1.00	–	–
Change	2.62 (1.12, 6.18)	4.88 (1)	0.027
Number of infusions per duration stay ICU	1.11 (1.03, 1.19)	8.37 (1)	0.004
Duration of peripheral IVL	1.10 (1.02, 1.17)	6.87 (1)	0.009
Number of injections/24 hours	1.11 (1.03, 1.24)	4.03 (1)	0.045
Duration of CVL	1.07 (1.02,1.11)	8.83 (1)	0.003
Number of infusion via CVL	1.28 (1.01, 1.61)	4.11 (1)	0.043
Number of antibiotics given via CVL/24 hours	1.40 (1.20, 1.64)	17.92 (1)	0.001
Number of days antibiotics given IV	1.06 (1.02, 1.10)	8.55 (1)	0.003
Frequency Change CVL			
Not changed	1.00	–	–
Changed	8.13 (2.36, 28.06)	11.00 (1)	0.001

CI = Confidence Interval; df = degrees of freedom; A&E = accident and emergency department; OT = operation theater.

than that observed by Barba *et al.* (2006) (39%). The Malaysian study done by Rozaidi *et al.* (2001) was 23% and Hughes *et al.* (2005) was 13.9%. However, both the studies report prevalence rates and it is to be noted that incidence rates cannot be compared with prevalence rates. Hence, this study forms the first study on incidence from Malaysian hospitals.

Risk factors

All the risk factors identified for acquiring of ICU-associated NIs were directly or indirectly related to the usage of intravascular devices for long periods of time, to existing sepsis or MRSA carriage, or to associated disease conditions or treatment resulting in an immune-depressive state. Patients receiving infusions via CVC for a short duration had a lower risk of acquiring bacteremia when compared to those who received the same for longer durations (HR=1.071; CI=1.02,1.11; P = 0.03) in this study supporting the observations of Fernandez-Crehuet *et al.* (1997). In the current study, using survival analysis it was predicted that every additional day of usage of mechanical ventilation increased the risk of acquiring bacteremia by 25% in ICU patients (Table 2) suggesting that, longer usage of mechanical ventilation could contribute to bacteremia.

Patients who had MRSA in the axilla, groin, perineum, or throat had a 13 times higher risk of bacteremia compared to patients who did not have MRSA. This finding suggests that the presence of bacteria in susceptible parts of the body may be an indicator for potential bacteremia (HR = 9.61; CI = 2.76, 33.54; P = 0.001). This data suggests that insertion of a CVC in the femoral region can predispose a patient to bacteraemia, especially if the colonization status of the patient is unknown prior to the insertion. Thus femoral lines should be avoided if possible. This was also recommended in CDC (1994). Unsurprisingly, patients diagnosed with sepsis were more likely to be bacteremic. Hence early clinical signs and symptoms of sepsis should be considered a pre-warning sign of bacteremia.

Age did not appear to influence the acquisition of bacteremia in this study. However, other studies have reported a relation between increasing age and infection (Fernandez-Crehuet *et al.*, 1997; Salomao *et al.*, 2006; Girard & Wesley, 2007). This discrepancy could be because the patients recruited in this study belonged to a younger age group and were well nourished and experienced shorter stays in the ICUs (Katherason *et al.*, 2008).

One of the major risk factors identified for developing bacteremia was cancer: Patients who had pre-existing cancers had a three-fold greater risk of developing bacteremia compared to non-cancer patients. This could due to the underlying immune-depression in cancer patients and

Table 2. Predictors of Device-Associated Bacteremia in the ICUs using Multivariable Cox Proportional Hazard Model

Variable	Adjusted Hazard Ratio (95% *CI*)	Wald Stat (*df*)	*P* value
Cancer	3.50 (1.20, 10.20)	5.27 (1)	0.022
Hydrocortisone	5.58 (1.82, 17.16)	9.01 (1)	0.003
Duration of infusion CVC /IVC	0.74 (0.65, 0.92)	8.24 (1)	0.004
Duration of mechanical ventilation	1.25 (1.07,1.45)	7.82 (1)	0.005
Change CVC (changed/not changed)	0.00 (0.00, 0.06)	8.78 (1)	0.003
MRSA (axilla/perineum/ throat)	13.51 (2.42, 75.31)	8.81 (1)	0.003
Clinical sepsis	13.14 (2.51, 68.71)	9.31 (1)	0.002

CI = Confidence Interval; df = degrees of freedom.

to the frequent infusions they receive during chemotherapy. A similar phenomenon of increased risk of developing bacteremia (5-fold risk) was observed in patients receiving hydrocortisone therapy.

Bacterial Patterns in Malaysia

In the current study, the commonest organism causing bacteremia (10.7%) was *K. pneumoniae* and *Acinetobacter* species whereas the study done by Hughes *et al.* (2005) had highlighted *P. aeruginosa* and Methicillin-resistant *S. aureus* as the commonest bacteria causing bacteremia (23.4%). However, Rosaidi *et al.* (2001) showed *Acinetobacter species* and *S. aureus* as the commonest organism causing bacteremia (8.1%) in Malaysia.

The study done by Agarwal *et al.* (2006) in India observed that the organisms causing bacteremia to be *Acinetobacter* species (34.5%), *P. aeruginosa* (23.9%) and *Escherichia coli* (15.2%). Agodi *et al.* (2009) found *P. aeruginosa* (19.0%), *S. aureus* (9.4%) and *Acinetobacter baumannii* (7.5%) as the main organisms causing bacteremia. This study differs from other studies in that *K. pneumoniae* has been found in this study as a causative organism for bacteremia.

Prevention of Bacteremia

The above study highlights the patients that are most likely to develop nosocomial bacteremias and as such, greater focus toward proper infection control practices ought to take place when nursing these patients.

Many modifiable factors have been shown to increase the risk of catheter-related bloodstream infections. These include lapses in the use of strict sterile techniques in the insertion of central venous catheters and insertion of catheters into internal jugular or femoral vein sites. In 1996, the CDC developed guidelines for the prevention of intravascular device-related nosocomial infections. In these guidelines, the corrective approach involves frequent in-service education (Eggimann & Pittet, 2002), frequent encouragement, and motivation for health care workers in ICUs, including specific guidance in changing habits and frequent NI audits. This in service-education suggested are the training of health care workers in the procedures for the insertion and maintenance of intravascular devices and appropriate infection control measures to prevent intravascular device-related infections.

Better hand washing practices, avoiding the misuse of gloves, the correct use of povidine solution for cleansing (Little *et al.*, 1999), and improved care of CVC connections and hubs for injections appear to be the most important practices that could reduce the occurrence of nosocomial bacteremia. Thus, the ICU staffs need to be continually reminded about the proper procedures required to comply with the correct steps and timing in hand washing. Simple programmes, such as *Henry the Hand*, and the use of hand washing signals can aid ICU staff members in the prevention of bacteremia and NI.

Gloves are worn to reduce the likelihood that microorganisms present on the hands of personnel will be transmitted to patients during invasive or other patient-care procedures that involve touching a patient's mucous membranes and non-intact skin. However, wearing gloves does not replace the need for hand washing because gloves may have small, non-apparent defects or may be torn during use, and hands can become contaminated during removal of gloves. Failure to change gloves between patient contacts is an infection control hazard.

The most effective technique for controlling nosocomial bacteremia and NI in the three ICUs is to strategically implement quality assurance (quality control, or QC) measures. An important element of the QC is to implement evidence-based management. Evidence-based management can be a feasible approach that changes past healthcare practices into quality and patient care standards.

The present study highlights the incidence and predictors for acquiring nosocomial blood infections in three ICUs

in three major hospitals in Malaysia. The incidence was reported for the first time from Malaysia and was observed to be 29.3%. The bacterial profile differed from that reported earlier in that the highest causative organisms were found to be *K. pneumoniae*. The predictors of being bactereamic using Cox Proportional Hazard Regression Model analysis are duration of use of IVC devices and ventilators, an initial diagnosis of sepsis, pre-existing conditions such as cancer, presence of MRSA, and administration of hydrocortisone drugs. The results suggest that persistent high levels of nursing interventions and medical care in combination with severity of illness and prolonged use of intravascular devices are associated with the acquisition of nosocomial bacteremia in critically ill patients in ICUs. Such infections are responsible for higher mortality, prolonged stay, and increased therapeutic activity independent of the initial severity of illness. We suggest that strategic implementation of quality assurance measures be conducted in the ICUs, along with frequent in-service education. Specific guidance in changing habits, frequent surveillance, and NI audits should be performed effectively and persistently in all of the ICUs. This would improve the long term effect on control of ICU-associated NIs.

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REFERENCES

Agarwal, R., Gupta, D., Ray, P., Aggarwal, A.N. & Jindal, S.K. (2006). Epidemiology, risk factors and outcome of nosocomial infections in a Respiratory Intensive Care Unit in North India. *Journal of Infection* **53**: 98–105.

Agodi, A., Auxilia, F., Barchitta, M., Brusaferro, S., D'Alessandro, D., Montagna, M.T., Orsi, G.B., Pasquarella, C., Torregrossa, V., Suetens, C., Mura, I., (2009). Building a benchmark through active surveillance of intensive care unit-acquired infections: the Italian network SPIN-UTI *Journal of Hospital Infection*. Nov 13. 18th European Congress of Clinical Microbiology and Infectious Diseases, Barcelona, Spain. Available at: http://www.blackwell publishing.com. Date accessed: 01 Nov. 2009.

Barba, E.J.R., Rosenthal, V.D., Higuera, F., Oropeza, M.S., Torres Herna´ndez, H., Martha Sa´nchez Lo´pez, M.S., Lona, E.L., Duarte, P., Ruiz, J., Hernandez, R.R., Chavez, A., Cerrato, I.P., Ramirez, G.E. & Safdarg, N. (2006). Device-associated nosocomial infection rates in intensive care units in four Mexican public hospitals Me´xico City and Guanajuato, Mexico; Buenos Aires, Argentina; and Madison, Wisconsin by the Association For Professionals in Infection Control and Epidemiology, Inc. doi:10.1016/j.ajic.2005.05.024244

Centers for Disease Control and Prevention (1994). Guidelines for prevention of nosocomial pneumonia. *Infection Control and Hospital Epidemiology* **5**: 587–627.

Crnich, C.J. & Maki, D.G. (2002). The promise of novel technology for the prevention of intravascular device–related bloodstream infection. Part I. Pathogenesis and short term devices. *Clinical Infectious Diseases* **34**: 1362–1368.

Eggimann, P. & Pittet, D. (2002). Overview of catheter-related infections with special emphasis on prevention based on education programs. *Clinical Microbiology Infect*ion **8(5)**: 295–309.

Fernandez-Crehuet, R., Diaz-Molina, C., de Irala, J., Martinez-Concha, D., Salcedo-Leal, I. & Masa-Calles, J. (1997). Nosocomial infection in an intensive care unit, identification of risk factors. *Infection Control Hospital Epidemiology* **18**: 825–830.

Girard, T.D. & Wesley, E. (2007). Bacteremia and sepsis in older adults. *Clinics in Geriatric Medicine* **23**: 633–647.

Hughes, A.J., Ariffin, N., Huat, T.L., Abdul Molok, H., Hashim, S., Sarijo, J., Abdul Latif, N.H., Abu Hanifah, Y. & Kamarulzaman, A. (2005). Prevalence of nosocomial infection and antibiotic use at a University Medical Center in Malaysia. *Infection Control Hospital Epidemiology* **26**(1): 100–104.

Katherason, S., Naing, L., Jaalam, K. & Ismail, A. (2008). Baseline assessment of intensive care-acquired nosocomial infection surveillance in three adult intensive care units in Malaysia. *The Journal of Infection in Developing Countries*. Available at: http://www.jidc.org/index.php/journal/article/view/19745504/107. Date accessed: 01 Nov. 2009.

Laporan Hospital Ipoh (2005). Hospital Ipoh, Ministry of Health, Perak, Malaysia.

Laporan Hospital Universiti Sains Malaysia (2006). Hospital Universiti Sains Malaysia, Kubang Kerian, Kelantan.

Little, J.R., Murray, P.R., Traynor, P.S. & Spitznagel, E. (1999). A randomized trial of povidone-iodine compared with iodine tincture for venipuncture site disinfection: effects on rates of blood culture contamination. *American Journal Medicine* **107**(2): 119–125.

Magadia, M.D., Raul, R., Melvin, P. & Weinstein, M.D. (2001). Laboratory diagnosis of bacteremia and fungemia. *Infectious Disease Clinics of North America* **15**(4): 1009–1024.

National Nosocomial Infectious Surveillance (NNIS, 2004) System Report, data summary from January 1992 thorough Jun, 2004, issued October 2004. *American Journal of infectious Control* **32(8)**: 470–485.

Reimer, L.G., Wilson, M.L. & Weinstein, M.P. (1997). Update on detection of bacteremia and fungemia. *Clinical Microbiology Review* 444–465.

Rozaidi, S.W., Sukro, J. & Dan, A. (2000). The incidence of nosocomial infection in the intensive care unit, Hospital Universiti Kebangsaan Malaysia: ICU acquired nosocomial infection surveillance program 1998–1999. Faculty of Medicine, Hospital Universiti Kebangsaan Malaysia, Cheras, Kuala Lumpur, Malaysia.

Salomao, R., Alvarez-Moreno, C., Mehta, Y., Higuera, F., Cuellar, L.E., Arikan, O.A., Abouqal, R. & Leblebicioglu, H. (2006). Device-associated nosocomial infections in 55 intensive care units of 8 developing countries. *Annals of Internal Medicine* **145**(8): 581–591.

Tan, P.S.K. (1998). *Infection Watch*. University Malaya Medical Center, Kuala Lumpur, Malaysia.

Weinstein, M.P., Towns, M.L., Quartey, S.M., Mirrett, S., Reimer, L.G. & Parmigiani, G. (1997). The clinical significance of positive blood cultures in the 1990s: A prospective comprehensive evaluation of the microbiology, epidemiology, and outcome of bacteremia and fungemia in adults. *Clinical Infectious Dis*ease **24**(4): 584–602.