ORIGINAL ARTICLE

The Incidence of Nosocomial Infection in the Intensive Care Unit, Hospital Universiti Kebangsaan Malaysia: ICU-acquired Nosocomial Infection Surveillance Program 1998-1999

S W Rozaidi, J Sukro, A Dan, Department of Anaesthesiology & Intensive Care, Faculty of Medicine, Hospital Universiti Kebangsaan Malaysian, Jalan Tenteram, Bandar Tun Razak, Cheras, 56000 Kuala Lumpur

Summary

CU-acquired nosocomial infection (NI) remains one of the major causes of ICU mortality. This study presents the incidence of ICU-acquired nosocomial infection in ICU HUKM for the years 1998 and 1999, as part of the ongoing ICU-acquired nosocomial infection surveillance program. The overall incidence was 23%. The main types of NI was lower respiratory tract infection (15.3%), primary bacteraemia (8.1%), ventilator associated pneumonia (5.4%), urinary tract infection (2.0%), skin infection (1.6%) central venous catheter sepsis (1.2%) and surgical skin infection (0.8%). The overall culture positive nosocomial infection rate was only 12.1%, majority from the lungs (12.6%), blood (7.3%), skin swabs (2.0%), and urine (1.6%). The main gram-negative organism cultured was *Acinetobacter sp.* (19%) and *Staph. aureus* (8.5%) was the gram-positive organism. The overall ICU mortality rate was 27.5% of which 60.9% of patients who died were attributed directly to sepsis.

Key Words: ICU-acquired nosocomial infection, Nosocomial infection, Intensive care unit, Incidence, Infection rate, Microorganism, Lower respiratory tract infection, Ventilator associated pneumonia, Primary bacteraemia, Skin infection, Epidemiology

Introduction

One of the major causes of ICU mortality and morbidity is nosocomial infection (NI)[1,2]. These infections not only adversely affect the ICU patient's outcome but they also pose a financial burden to both patients and hospital as well increasing overall medical costs[3,4].

There are several ways of decreasing the incidence of NI in the ICU[5]. The Study on the Efficacy of Nosocomial Infection Control Programs (SENIC) had demonstrated that a well-run infection control programmes coupled with surveillance could decrease NI by 32%[5]. Furthermore, the prevention of infection in the ICU requires clinicians to have knowledge of

infection rates, source and nature of infection, as well as the anti-microbial resistance patterns found in their own ICU.

Currently hospital-acquired infections in developed countries occur in 2 to 6% of hospitalised patients[6,7], whereas in developing countries, the rates are higher, some reaching as high as 25%[8,9]. These figures depend on the methods used for detecting NI and the variables used in determining such rates[4].

In order to be able to gauge and assess whether policies and programs implemented are able to reduce the incidence of NI, we must first have the "local" incidence or prevalence rate of ICU-NI.

The ICU HUKM is a 24-bed general ICU located in a 1600-bed university hospital. Both surgical and medical cases are managed in the ICU. The ICU is run by the Department of Anaesthesiology and Intensive Care on a 'semi-open' concept where patient is co-managed by both the referring unit and ICU doctors.

The "ICU-acquired nosocomial infection surveillance programme" in HUKM was first started in January 1998 with the help of the HUKM Infection Control Committee, which carries out its ICU rounds on a daily basis, where microbiological data including sensitivity patterns are presented and discussed during the rounds. It is currently into its third year of surveillance.

This report the first of its kind in Malaysia, describes the epidemiology of NI in the first two years of implementation of the surveillance programme in an adult general medical and surgical ICU in HUKM.

Materials and Methods

Starting from the month of January 1998, information from each adult patient admitted into the ICU was collected for the purpose of ICU-acquired nosocomial infection surveillance.

The information collected included patient demographics (age, sex, race), diagnosis, reason for ICU admission, and their disciplines (medical, surgical). All data concerning the number and duration of devices used (central venous catheters, pulmonary catheters, indwelling urinary catheters, mechanical ventilation etc.) as well as number of device days were documented. The use of anti-microbial agents, status of feeding (enteral, parenteral), and agents for stress ulcer prophylaxis were included in the surveillance. We also recorded the development and duration of shock (of all aetiologies) in these patients, as well as the choice of vasopressors/inotropes used.

There are basically two forms of cultures done in our ICU; routine and specific cultures. Tracheal aspirate and urine cultures are routinely done as part of the "ICU-acquired nosocomial infection surveillance programme". The tracheal aspirates are taken for all intubated patients with or without mechanical ventilation on the day of admission, and on every Tuesday and Thursday. Urine cultures are taken for all patients on continuous bladder drainage (CBD) on day one of CBD usage and thereof once per week. No routine urine cultures were done for non-catheterised patients. As for specific cultures, the ICU clinicians in charge of the patient depending on their own clinical judgement and discretion order such cultures.

The ICU staff nurses according to set ICU protocol and procedures take all routine cultures. The tracheal aspirates are taken under aseptic conditions with two staff nurses performing the procedure. One staff nurse helps in securing the endotracheal or tracheostomy tube (ETT) while the other performs the act of tracheal aspirate by inserting a suction catheter connected to a sterile collection container into the trachea without suctioning being applied. The catheter is advanced until resistance is felt. At this point suctioning is applied while the catheter is slowly withdrawn from the airways and ETT. Once the catheter is removed from the ETT, the residual

secretion in the catheter tubing is further expelled from the tubing by suctioning sterile water. The specimen container is then labelled and sent for cultures.

Urine samples are taken via the specimen port connected to the CBD tubing. Povidine solution is applied to the port, and a sterile 10ml syringe with a 23G needle connected is used to collect the urine. The urine is then placed into a sterile container and sent for cultures and sensitivity.

The ICU doctors perform blood cultures under aseptic condition. The site of venupuncture is cleaned with povidine and spirit and draped with sterile cloth. A sterile 10ml syringe with a 23G needle is used to aspirate 10ml of blood. This blood (after changing to a new needle) is then injected into two culture bottles (Bactec™) aerobic and anaerobic culture bottles) and sent to the laboratory for culture and sensitivity. If a new central venous line (CVC) or arterial line is inserted, and blood cultures are required, the blood specimen is then taken from these catheters directly and injected into the culture bottles as these lines are inserted under aseptic condition.

Patients suspected of having CVC sepsis will have three samples taken, one, blood from a vein away from the CVC site, another blood sample directly from the CVC lumen itself, and the third specimen being the CVC tip itself, all done under aseptic technique. The CVC tips were processed according to the method by Maki *et al*[10].

A sterile swab stick is used to collect specimens of suspected skin and / or wound sepsis and placed into a sterile container.

Patients diagnosed clinically with pneumonia had a fiberoptic bronchoscopic examination and broncho-alveolar lavage (BAL) performed on them. The site (lung lobes or segments) for bronchoscopy is initially determined by identifying suspected lung infected areas on chest radiography. Once the bronchoscopy tip is in place, sterile water in aliquots of 50ml (to a total of 200mls) is injected into the side port of the bronchoscope and subsequently aspirated into a sterile collecting container. A total of four containers will then be sent for cultures.

Samples sent to the microbiology laboratory will undergo microscopic examination, incubation, Gram staining and subculture for organism identification and sensitivity testing. Tracheal aspirates samples would further be microscopically examined for pus cells under 100 X magnification and graded into either scanty pus cells (< 4 pus cells per microscope field); moderate pus cells (5 - 10 pus cells per field) and numerous pus cells (> 10 pus cells per field). The details on how such microbiology testing is carried out is available in most microbiology reference books and will not be further discussed in this paper. All culture growth is recorded as light (< 15 colonies), moderate (sub confluent growth), and heavy (confluent growth).

Definitions

Infection, bacteraemia, sepsis, severe sepsis and septic shock

The definitions of the above were in accordance with the Consensus Conference of the American College of Chest Physicians and Society of Critical Care Medicine[11].

Infection is defined as a microbial phenomenon characterized by an inflammatory response to the presence of microorganisms or the invasion of normally sterile host tissue by those organisms. Bacteraemia is defined as the presence of viable bacteria in the blood.

Sepsis is the systemic response to infection. It is manifested by two or more of the following conditions as a result of infection: temperature >38°C or <36°C; heart rate > 90 beats/min; respiratory rate > 20 breaths/min or $PaCO_2$ < 4.3kPa (<32 Torr); white blood cell count > 12 000 cells/mm^3, or > 10% immature (band) forms. Severe sepsis is sepsis associated with organ dysfunction, hypoperfusion or hypotension.

Hypoperfusion and perfusion abnormalities may include but are not limited to, lactic acidosis, oliguria or an acute alteration in mental status. Septic shock is sepsis with hypotension, despite adequate fluid resuscitation, along with the presence of perfusion abnormalities may include, but are not limited to, lactic acidosis, oliguria or an acute alteration in mental status. Patients who are on inotropic or vasopressors agents may not be hypotensive at the time when perfusion abnormalities are measured.

Culture positive samples

A microbiologist classifies all samples with positive growth of organism into 'significant', 'colonizer', 'normal flora' or 'contamination'. These growths are recorded as light (<15 colony-forming units), moderate (sub confluent growth) or heavy (confluent growth).

All positive blood cultures are considered clinically significant when a known pathogen is cultured coupled with clinical evidence of sepsis is present. The isolation of an organism from one or more bottles was accepted as being clinically significant for all organisms except coagulase-negative staphylococci, where isolation of two or more bottles were required before considering it as significant given the fact of its high propensity to contaminate blood cultures.

The clinical diagnosis of infection or sepsis is left to the ICU clinician based on his or her own assessment and judgement while taking into account the definitions for infection[12]. Usually a high index of suspicion is required before any new fever or sepsis is deemed to be due to a new infection. For example nosocomial pneumonia is suspected when a patient previously asymptomatic develops crackles on auscultation or dullness to percussion on chest examination coupled with new onset of purulent sputum and chest radiographic examination showing new or progressive infiltration, consolidation, cavitations or pleural effusion. The diagnosis is further supported with positive organism cultured from blood cultures; isolation of pathogen from specimen obtained by transtracheal aspirate, bronchial brushing or broncho-alveolar lavage.

Pneumonia was considered ventilator associated (VAP) when its onset occurred after 48 hours of mechanical ventilation (MV) and was judged not to have been incubated before starting MV, coupled with high clinical suspicions. When possible, a fiberoptic bronchoscopic examination and broncho-alveolar lavage (BAL) was performed on each of these patients suspected to have VAP within the first 24 hours after the development of a new pulmonary infiltrate. Lower respiratory tract infections are all other forms of respiratory infections that are not due to pneumonia e.g. bronchitis, tracheobronchitis, tracheitis.

Patients are suspected to have primary bacteraemia/sepsis when they develop a new onset of fever with or without increase in total white, as well as an apparent change in their overall condition such as hypotension, tachycardia and increasing blood lactate levels but with no other recognized cause (patients with central venous catheter infection are excluded from this group).

Any patient with cloudy foul smelling urine with or without suprapubic tenderness is suspected to have a urinary tract infection, while central venous line sepsis is suspected in any patients with evidence of sepsis together with local inflammation (cellulitis) and pus production from the CVC insertion site. A positive culture for CVC sepsis is said to have occurred when all three cultures taken grows the same organism.

ICU-acquired nosocomial infection (NI)

The diagnosis of an NI was done according to the standard definitions of the Centres for Disease Control and Prevention (CDC)[12] where there must be no evidence that the infection was present or incubating at the time of ICU admission. We further defined an ICU-acquired infection as an

infection developing 24-hours after ICU admission having originated in the ICU, and being actively treated. All patients diagnosed to have either community-acquired or hospital-acquired (non-ICU) infections were excluded.

Clinical Nosocomial Infection Rate (CNIR)

Defined as, the number of patients diagnosed clinically with NI per 100 patients admitted into the ICU. In specific NI e.g. Nosocomial lower respiratory tract infection (NLRTI), the CNIR is defined as, the number of patients diagnosed clinically with NLRTI per 100 patients admitted into the ICU.

Culture Positive Nosocomial Infection Rate (CPNIR)

Defined as, the number of patients diagnosed with NI having positive culture samples per 100 patients admitted into the ICU. In specific NI e.g. Nosocomial lower respiratory tract infection (NLRTI), the CNIR is defined as, the number of patients diagnosed clinically with NLRTI per 100 patients admitted into the ICU.

Device-use rates[6]

Defined as, the number of device-days divided by the number of patients-days.

$$\text{Example: DU} = \frac{\text{Number of device-days}}{\text{Number of patient-days}}$$

Device-associated infection rate[6]

Defined as, the number of device-associated infections for a specific site per 1000 device-days.

Example:
VAP rate per 1000 ventilated days

$$= \frac{\text{Number of ventilator-associated pneumonia}}{\text{Number of ventilated days}} \times 1000$$

*For details on how to calculate the 'device-days' and 'patient-days', readers are advised to refer to the National Nosocomial Infections Surveillance Report[6].

Statistical analysis

Data are either expressed as frequency, proportion, percentage or means with standard deviation (SD). Significance test for comparing two or more proportions from independent groups are analysed using the Chi-square test (Yates correction for continuity was used for 2 by 2 tables), where else comparison of means (t-test) is used for data presented as means ± SD (MedCalc® Version 5.00.013 - Windows 95/98/NT Copyright® 1993-1999 Frank Schoojans). A 'P value' of less than 0.05 ($P < 0.05$) was considered statistically significant.

Results

A total of 988 adult patients were admitted into the general intensive care unit (ICU) during the years 1998 and 1999, of these 23% developed NI (Table I). Majority of those admitted were from surgical -based disciplines (74.9%) including both post-operative elective and emergency surgical cases. Nearly a third (31.6%) were admitted for post-operative care and monitoring without mechanical ventilatory support. A significant percentage, 11.4% were admitted with sepsis and septic shock. Over 35% of the medical cases admitted into ICU developed NI as compared to 16% of the surgical cases. None of the Obstetric & Gynaecology and ENT patients developed NI.

Nearly 60% of patients admitted were males, with majority Malays (55.1%) followed by Chinese (34%) and Indians (8.5%). The sex and racial distribution for patients developing NI were similar to the ICU demographics.

The average age of the ICU patients was 47 ± 18 years old with majority in the 41 to 60 years age group (35.2%). The patients with NI were slightly older, 50 ± 16 years old but with majority in the 41 - 60 years age group (40.3%).

Table I
Demographics of Patients Admitted into the Intensive Care Unit

	Overall Patients n (%)	Patients with Nosocomial Infection n (%)
Total number of patients	988	228 (23.1)
SEX		
Male	588 (59.5)	144 (63.2)
Female	400 (40.5)	84 (36.8)
RACE		
Malay	544 (55.1)	136 (59.6)
Chinese	336 (34.0)	68 (29.8)
Indian	84 (8.5)	20 (8.8)
Others	24 (2.4)	4 (1.8)
AGE (mean ± SD)	47 ± 18	50 ± 16
< 21 years	100 (10.1)	16 (7.0)
22 - 30 years	132 (13.4)	28 (12.3)
31 - 40 years	136 (13.8)	20 (8.8)
41 - 60 years	348 (35.2)	92 (40.3)
> 61 years	272 (27.5)	72 (31.6)
DISCIPLINE		
Surgery	344 (34.8)	96 (42.1)
Neurosurgery	260 (26.3)	48 (21.1)
Orthopaedics	64 (6.5)	4 (1.7)
ENT	52 (5.3)	0 (0.0)
Medical	156 (15.8)	56 (24.6)
Obstetric And Gynaecology	44 (4.5)	0 (0.0)
Others**	68 (6.8)	24 (10.5)
REASON FOR ICU ADMISSION		
Cardio respiratory arrest	28 (2.8)	12 (5.2)
Pure respiratory arrest	120 (12.1)	40 (17.5)
Pneumonia	40 (4.0)	24 (10.5)
Cerebral protection	168 (17)	32 (14.0)
Airway protection	8 (0.8)	8 (3.6)
Post operative ventilation	160 (16.2)	32 (14.0)
Post operative care	312 (31.6)	32 (14.0)
Sepsis	48 (4.9)	8 (3.6)
Septicaemic shock	64 (6.5)	32 (14.0)
Close monitoring	40 (4.0)	8 (3.6)

The percentage is calculated per each individual group (i.e. 'overall' and 'nosocomial infection')

*** Others are including plastic surgery, urology, nephrology, neuromedical and endocrinology patients*

Table II
Types of ICU-acquired Nosocomial Infection

Types on Nosocomial Infection	Frequency (%)
Overall	228 (23.1)
Lower respiratory tract infection	151 (15.3)
Primary bacteraemia	80 (8.1)
Pneumonia	53 (5.4)
Urinary tract infection	20 (2.0)
Skin infection	16 (1.6)
Central venous catheter infection	12 (1.2)
Surgical skin infection	8 (0.8)
* Others	12 (1.2)

Frequency = number of patients diagnosed with nosocomial infection

Percentage = the number of patients diagnosed with nosocomial infection per total ICU admission (988 patients)

** Others includes intra-abdominal and gastro-intestinal infections*

The main types of NI found are presented in Table II.

A total of 2252 samples from various sites were taken from 560 patients (56.7%). Patients may have had several cultures done on them during their admission in ICU. Seven hundred and fifty-six samples (out of the 2252 samples) were taken from 228 patients clinically diagnosed to have NI, of which, 572 samples from 120 patients were culture positive. This gave a Positive Culture Nosocomial Infection Rate of 12.1% with nearly 50% of patients clinically diagnosed NI having negative cultures. The Gram-negative organisms constituted 75% of nosocomial microorganisms cultured. Nearly 19% were *Acinetobacter sp.*, followed by *Klebsiella sp.* (17.2%) and *Pseudomonas sp.* (14.3%). Of the Gram-positive organisms, MRSA (methicillin-resistant *Staphylococcus aureus*) (7.4%) remains the highest number cultured in patients with NI. This was followed by MRSE (multi-resistant *Staph. epidermidis*) (3.2%). Candida sp. mainly arising from the urine consisted of 1.6% of total samples cultured positive (Table III).

The Clinical Nosocomial LRTI Rate = 15.3% and the Culture Positive Nosocomial LRTI Rate = 10.5%, therefore nearly 31% of the cultures done in these patients were negative. The three main organisms causing nosocomial LRTI were *Acinetobacter sp.* (28.9%); *Pseudomonas sp.* (28.9%), of which 77% were *Pseudomonas aeruginosa*) and MRSA (9.2%). (Table III) Out of the 151 patients clinically diagnosed with nosocomial LRTI, only 16 patients (10.6%) were not mechanically ventilated.

Eighty patients were diagnosed to have primary bacteraemia (Clinical Nosocomial Bacteraemia Rate = 8.1%), of these the number of culture positive blood samples was 144 in 60 patients giving a Positive Culture Nosocomial Bacteraemia Rate of 6.1%. Majority of organisms cultured were Gram-negatives such as *Klebsiella sp.* (25.7%), followed by *Acinetobacter sp.* (22.9%), and *Strenotrophomonas sp* (11.4%). The Gram-positive organisms were mainly MRSE (11.4%). MRSA (5.7%) and *Strep. viridans* (5.7%) of the total organisms cultured in the blood.

Twelve patients were diagnosed to have central venous catheter sepsis (Clinical Nosocomial Catheter Sepsis Rate = 1.2%). The Culture Positive Nosocomial CVC Infection Rate was 1.2%. We had equal numbers of Gram-positive and Gram-negative organisms cultured in patients with CVC NI. These were Acinetobacter sp. (50%) and MRSE (50%). The Device-use rate for CVC's were 0.71. The mean duration of time the CVC were in use for these patients was 28.8±5.81 days as compared to 17.6±15.71 days in patients who did not develop CVC bacteraemia (P = 0.0139). The CVC-associated blood stream infections (BSI) were 2.5 patients per 1000 catheter days. (Table IV)

The Clinical Nosocomial UTI Rate was 2.0% and the Culture Positive Nosocomial UTI Rate was 1.6%. *Klebsiella sp.* (75%) was the only bacterial organism

that contributed to the infection. The remaining 25% was attributed to *Candida sp.* All the patients with NI had an indwelling urinary catheter (CBD) in place at the time of developing the NI. None of the patients without a catheter developed any form of UTI. The Device-use rate for CBDs was 0.79, and the catheter-associated UTIs were 2.9 patients per 1000 catheter days. (Table IV)

Most of the skin swabs (75%) taken were from burns patients. Out of the 24 positive cultures received from these burns patients, 50% had MRSA. The main Gram-negative organisms cultured were *Klebsiella sp.* (16.7%), *Enterobacter sp.* (16.7%) and *Enterococcus sp.* (16.7%). There were eight positive cultured skin swabs taken from surgical skin sites in patients diagnosed with intra-abdominal sepsis. Of these, Acinetobacter sp. and *Klebsiella sp.* (50% respectively) were the two main organisms cultured.

One hundred and eighty-eight patients with NI were ventilated (26.1% of all ventilated patients). The Device-use rate was 0.65. The average duration of ventilation for NI patients was 13±12.5 days as compared to non-NI patients, 3±2.1 days

Table III
Organisms Responsible for Nosocomial Infections in ICU

ORGANISM	*Overall	**LRTI	**Pneumonia	**Primary Bacteraemia	**CVC Sepsis	**UTI	*Skin *Infection	**SSI	**Other
	% (n=572)	%, (n=304)	% (n=28)	% (n=140)	% (n=16)	% (n=16)	% (n=32)	% (n=8)	% (n=8)
Acinetobacter sp.	19.0	28.9	42.8	22.9	50.0	0	12.5	0	0
Pseudomonas sp.	4.2	6.6	0	0	0	0	0	0	0
Pseud. aeruginosa	14.7	22.3	0	2.9	0	0	0	0	20.0
Klebsiella sp.	17.2	21.1	28.6	25.7	0	75.0	12.5	50.0	0
Strenotrophomonas sp	2.1	0	0	11.4	0	0	0	0	0
Enterobacter sp.	3.2	3.9	0	5.7	0	0	12.5	0	0
Flavimonas sp.	0.5	0	0	2.9	0	0	0	0	0
MRSA	7.4	9.2	14.3	5.7	0	0	37.5	0	20.0
Staph. aureus	1.1	2.6	0	0	0	0	0	0	0
Staph. epidermidis	1.1	2.6	0	0	0	0	0	0	0
MRSE	3.2	0	0	11.4	50.0	0	0	0	0
Strep. viridans	1.6	1.3	0	5.7	0	0	0	0	0
Enterococcus sp.	1.1	0	0	2.9	0	0	12. 5	0	0
Clostridium deficile	1.1	0	0	0	0	0	0	0	40.0
Candida sp.	1.6	1.3	14.3	0	0	25.0	0	0	0
Others	1.1	0.2	0	2.9	0	0	0	0	0

** Results are presented as percentages: x' organism per site X 100% / Total 'x' organism per site*

*** Percentage: Number of organism X 100% / Total number of organism*

LRTI =Lower respiratory tract infection.
CVC =Central venous catheter.
UTI =Urinary tract infection.
SSI =Surgical skin infection.

Table IV
Device-use Ratio (DU) and Device-associated Nosocomial Infections Rates for Mechanical Ventilation, Urinary Catheters, and Central Venous Catheters in the ICU, HUKM Compared with ICU, Jordan University Hospital (JUH) and National Nosocomial Infections Surveillance (NNIS)

Parameter	HUKM Rate	JUH Rate	NNIS Rates (mean/median)	Percentile Compared with NNIS
Mechanical ventilation				
DU	0.65	0.46	0.38/0.37	> 90
VAP	11.9	19.1	11.3/10.1	< 75
Urinary catheter				
DU	0.79	0.75	0.75/0.76	< 75
UTI	2.9	15.6	5.2/5.1	< 25
Central venous catheter				
DU	0.71	0.47	0.47/0.47	> 90
CVC	2.5	3.0	4.5/4.6	< 50

VAP = ventilator associated pneumonia rate
UTI = urinary catheter associated-infection rate
CVC = central venous catheter-associated infection rate

(P<0.0001) (Table IV). Ventilated NI patients had a higher mortality rate when compared to ventilated non-NI patients (46% versus 34.6% respectively; P=0.0066). A total of 53 patients were diagnosed clinically to have ventilator-associated pneumonia (VAP) but only 28 patients were confirmed VAP based on the BAL results. The other 25 patients diagnosed VAP could not have their diagnosis supported by a BAL because of the unavailability of the bronchoscope during their admission. The incidence rate for VAP in patients who had BAL confirmation was 6.3 patients per 1000 ventilated days, while the overall incidence rate of VAP taking account those who did and did not have a BAL was 11.9 patients per 1000 ventilated days. (Table IV) (Table V)

Table V
Duration of Mechanical Ventilation and the Mortality Rate

	Mechanical Ventilated Patients with Nosocomial Infection (n = 200)	Mechanical Ventilated Patients with No Nosocomial Infection (n = 520)
Total days	2528	1416
Mean (days) ± SD	13 ± 12.5	3 ± 2.1
Mortality (%)*	92 (46.0)	180 (34.6)

**Percentage: Number of mortality from each group X 100% / Frequency of each group*

p value is p < 0.0001 comparing mean days of ventilation for both groups of patients.
p value is p = 0.0066 comparing mortality for both groups of patients.

The main Gram-negative organisms causing VAP were *Acinetobacter sp.* (42.8%), and *Klebsiella sp.* (28.6%). MRSA (14.3%) were the only Gram-positive organism causing VAP. Candida sp. made up of the remaining 14.3% organism detected.

A total of 284 patients (28.5%) had shock in ICU, of these, 112 patients (39.4%) were patients diagnosed to have NI (Group A). (Table VI) The average duration of shock in patients with NI was 7±7.1 days, as compared to non-NI patients (Group A_2), 3±1.7 days (P^A<0.0001). The mortality rate in these patients with shock however reflected differently between the two groups. Patients with no NI tended to have a higher mortality rate (81.4% versus 64.3%; P^{A2} = 0.0027).

Eighty-four (75%) NI patients had septic shock (Group B). These patients had an average ICU stay of 8±7.5 days as compared to Non-NI patients with septic shock (Group B_2) having 3±1.9 days (P^B<0.0001). The mortality rate for the Group B patients also differed, 61.9% for NI patients in septic shock versus 92% in non-NI patients in septic shock (P^{B2}<0.0005).

The average duration of non-septic shock patients with NI (Group C) was 4±4.9, as compared to non-NI patients (Group C_2), 2±1.3. This was highly significant (P^C=0.0018). However there was no statistical differences seen when the mortality rate was compared between the Group C patients (71.4% versus 66.7%; P^{C2}=0.8330).

The length of ICU stay differed between patients with NI and those without (13±12.4 days versus 3±2.8 days; P<0.0001). It was noted that patients with NI also had a higher mortality rate (40.4% versus 23.7%; P<0.0005). These patients th[illegible] had longer ICU stay (21.06±11.24 days 12.27±11.34 days; P < 0.0001) when compar[illegible] those without NI (Table VII). The mortality ra[illegible] NI patients when compared to the gen[illegible] population was 9.3% (the overall ICU mortal[illegible]

Table VI
Duration of Shock and the Mortality Rate in ICU Patients with Nosocomial Infection (NI) and No-nosocomial Infection

	Patients with NI in Shock (Group A)	Patients with NI in Septic Shock (Group B)	Patients with NI in Non-Septic Shock (Group C)	Patients with No NI in Shock (Group A_2)	Patients with No NI in Septic Shock (Group B_2)	Patients with No NI in Non-Septic Shock (Group C_2)
Frequency	112	84	28	172	100	72
Total days	784	672	112	488	312	176
Mean (days)	7	8	4	3	3	2
SD	7.1	7.5	4.9	1.7	1.9	1.3
p value*	p^A < 0.0001	p^B < 0.0001	p^C = 0.0018			
Mortality (%)	72 (64.3)	52 (61.9)	20 (71.4)	140 (81.4)	92 (92.0)	48 (66.7)
p value**	p^{A2} < 0.0027	p^{B2} < 0.0005	p^{C2} = 0.8330			

Percentage: $\frac{\text{Number of patients dead from each group X 100\%}}{\text{Frequency of each group}}$

* *p values comparing patients with nosocomial infection and patients with no-nosocomial infection Groups A, B and C's duration of shock.*

** *p values comparing patients with nosocomial infection and patients with no-nosocomial Groups A, B and C's mortality.*

Table VII
The Duration of ICU Admission and Mortality Rate

	Patients with Nosocomial Infections (n = 228)	Patients with No-nosocomial Infections (n = 760)
Total days	3044	2548
Mean (days) ± SD	13 ± 12.4	3 ± 2.8
Mortality (%)*	92 (40.4)	180 (23.7)
Total mortality days	6488	8340
Mean (mortality days) ± SD	21.06 ± 11.24	12.27 ± 11.34

** Percentage: Mortality from each group X 100% / Frequency of each group*

p value: $p < 0.0001$ comparing the means of ICU stay for both groups of patients.

p value: $p < 0.0005$ comparing mortality for both groups of patients.

p value: $p < 0.0001$ comparing the means of ICU stay for patients who died.

rate is 27.5%). Mortality directly attributed to sepsis was present in 56 patients with NI (60.9%). It is regretted that we were unable to determine the post-ICU hospital mortality.

There was no particular pattern noted when we compared the number of infection sites to mortality, ventilation days, shock days and LOS. The patients with three sites of infection tended to have a higher mortality rate (66.7%), those with two sites having longer ventilated days (mean 26 days) and those with four sites having longer duration of shock (mean 11 days), whilst the LOS was longest with patients having two infection sites (mean 24 days). Surprisingly there were no deaths in patients with five sites of infection.

Discussion

Nosocomial infection can involve any organ or system, particularly in those where instrumentation and device use is the highest e.g. urinary catheters, intubations and mechanical ventilation, central venous catheterisation etc. The relative incidences have generally remained constant over the years apart from differences in microorganism and anti-microbial sensitivity pattern[13].

In this paper, we did not specifically look at predisposing and risk factors leading to NI, neither did we attempt to discuss the antibiogram and organism sensitivity as this was thought to be beyond the scope of this paper. Despite data being collected on device usage, direct correlation testing was not performed as the major reason for this paper was looking at the incidence of NI in the ICU.

Currently there are two main significant and important studies on the epidemiology of ICU-acquired nosocomial infections available for comparison. These are the National Nosocomial Infections Surveillance System (NNIS)[6,14] and the European Prevalence of Infection in Intensive Care (EPIC) Study[15].

The NNIS is a database established in 1970 involving medical institutions in the United States of America conducted by the Hospital Infections Program to collect high quality nosocomial infection surveillance data that can be aggregated into a national database. The data available is published regularly allowing comparisons amongst institutions following NNIS methodology to be made.

The EPIC on the other hand is a 1-day prevalence study encompassing 1417 ICUs, providing a total of 10,038 completed case reports forms. It is the largest study of its kind in Europe.

The study conducted by the Jordan University Hospital (JUH)[16] was looking at the incidence rate of NI in their hospital comparing it with the NNIS group. This study allowed comparison to be made with a developing country, and as such would provide important results for comparison to be made against our study.

The overall NI rate in our institution was 23%, which was comparable to other similar ICUs (JUH group=16.2%, and 25% in a medical ICU in Saudi Arabia)[16]. In the EPIC study, the overall prevalence rate was 20.6% (ranging 9.7 to 31.6% depending on the ICU studied). Such difference seen in the prevalence rate in the EPIC study stems out from how each ICU views and conducts its infection policy and protocols. Even though it was not specifically looked at in the EPIC study but the differences between the prevalence rates noted amongst the various countries were thought to be due to differences in ICU practice.

Despite the high numbers of culture samples taken in our ICU patients, nearly 50% of the cultures from patients with NI were negative compared to only 15% in the EPIC study. Our low rates could be attributed to patients being on some form of anti-microbial prior to developing NI. The high positive culture rates in the EPIC study was thought to have reflected possible contamination of the sample or the process of colonization, which is a universal phenomenon in critically ill patients[15].

There were also differences in organisms cultured between the various studies. In the EPIC study the most frequently reported isolates were *Enterobacteriaceae* (34.4%) (Predominantly *Esch. coli, Klebsiella sp* and *Enterobacter sp.*) which was similar to other quoted studies[18]. In our study, *Acinetobacter sp.* (19%) was the predominant organism cultured. It was reported less than 6% in the NNIS, whilst for the Gram-positive group, *Staph. aureus* 8.5% (versus 30.1% in EPIC versus 10.9% in NNIS) remains the most frequent organism cultured.

The three main sites of NI in our patients were from lower respiratory tract (15.3%), primary bacteraemia (8.1%) and VAP (5.4%). Lower respiratory tract infections alone accounted for 66% of NI. The EPIC study noted pneumonia (47%), lower respiratory tract infections (18%) and UTI (18%) as their three main causes of NI in the ICU. The diagnosis used in this study as well as the JUH was based on the NNIS definitions, which itself used the CDC definitions[12].

Pneumonia and lower respiratory tract infections are the most common cause of NI in the critically ill patients but third commonest hospital NI after UTI and surgical wound infections[18]. It is difficult to determine precisely the incidence of nosocomial pneumonia in the ICU, as the clinical diagnostic criteria used have low specificity. The incidence ranges from 10% to 65%[19].

The most common organisms causing nosocomial pneumonia in the NNIS study are *Staph. aureus* (20%) and *Pseudomonas aeruginosa* (21%). In our own ICU this was not so. *Acinetobacter sp* were the predominant organism cultured (28.7%). This was very much higher when compared to the NNIS series (4.0%). At the time of writing this paper, preliminary results for the year 2000 still showed *Acinetobacter sp* as the major organism causing NI pneumonia. We were currently in the process of identifying why the incidence of this organism was high in our ICU (culturing of circuits, humidifier and dryers). Further more, such high incidences seen in our ICU may be the result of over diagnosing. The true frequency of NI cause by *Acinetobacter sp.* is difficult to assess because isolation of this organism in clinical specimens may reflect colonization rather than infection[20]. The distinction between the two in the critically ill patient may at times be difficult which may be the case for our high percentage as well as our unavailability to do BAL in all patients

diagnosed with pneumonia. What is known is that it is strongly associated with mechanically ventilated patients occurring in 4.0% to 26% of ventilated patients due to the moist environment of the ventilator circuits and humidifier[20]. As for other organisms, a recent prospective cohort study identified Staph. aureus (27%) as the most frequent organism causing nosocomial pneumonia[21] with 20% of patients dying within a week of the first positive culture. It was noted that those suffering from *Pseudomonas* sp pneumonia had a higher mortality rate (45% versus 14% from other organism)[21]. In our series 61.1% of patients with Pseudomonas sp pneumonia died compared to 32.6% dying from other organisms.

The incidence of clinically diagnosed VAP in our study was 11.9 patients per 1000 ventilator days (versus JUH =19.1). When compared to NNIS, our rates were less then the 75th percentile, thus considered a 'High' outlier where 75% of the hospitals in the NNIS database had lower rates (ratios) and 25% had higher rates (ratios) of VAP. This finding may point to a defect or problem in our care and technique of managing patients on mechanical ventilators. It could also reflect the high utilization of mechanical ventilation in our ICU (ventilator-device-use ratio of 0.65 ~ > 90th percentile of the NNIS database).

Our culture positive primary bacteraemia rate of 8.1% was very much lower then the NNIS rates of 17.0% but higher then the St. Thomas' Hospital group of 3.7%[13]. The differences could probably be under diagnosing of bacteraemia in our study. Patients may have been misdiagnosed to have systemic inflammatory response syndrome (SIRS) due to other causes rather then sepsis. The differentiation between SIRS and sepsis may be difficult in the critically ill patient with culture negative results. Further more, differences seen between various ICUs could be related to differences in laboratory culture techniques. We take more than one blood culture set from different sites to help exclude contamination but such techniques are not standard practice in most European hospitals[13]. In the EPIC study, laboratory culture techniques were not described. The pathogenesis of nosocomial blood-borne infection is commonly associated with prolonged use of intravascular devices such as central lines and dialysis catheters. The study by Maki *et al*[22] found that 21% of pulmonary artery catheters become colonized and that 1.1% of catheter insertions are associated with blood stream infection. Other studies have quoted colonization rates up to 60%[13]. The EPIC study further supports the high associated risk with intravascular devices. In our study such correlation was not sought but the CVC usage ratio in our ICU patients was 0.71, which was way above the 90th percentile of the NNIS. The incidence of colonization was also not available, as we do not send our CVC tips for routine cultures. Such high usage of CVC should logically attribute to higher infection rates, as most studies would indicate[3,13,23,24] but this was not so in our series. The CVC-associated infection was 2.5 patients per 1000 catheter days (<50th percentile of the NNIS; JUH = 3.0 patients per 1000 catheter days). Again the low incidence seen in our series was probably due to under diagnosing rather than 'true' favourable results.

Organisms commonly associated with catheter related sepsis are the gram-positive organisms i.e *Staph aureus* and *Staph. epidermidis*[24]. In the NNIS study, Coagulase-negative staphylococci (37%) were more commonly reported in central line associated sepsis in medical ICU. In our series, the two major gram-negative organisms cultured were *Klebsiella sp* (25.9%) and *Acinetobacter sp.* (22.9%) where as the NNIS group cultured only *Acinetobacter sp.* (2.0%), and *Klebsiella sp* (4.0%). Edgeworth JD *et al.*[13] had quoted the incidence of nosocomial bacteraemia in their series as *Acinetobacter sp* (2.0%) and *Klebsiella sp* (9.0%) with *Pseudomonas sp* (19%) still the highest gram-negative organism cultured, where else coagulase-negative staphylococcus (12%) the highest gram-positive organism cultured.

Surprisingly nosocomial UTIs did not occur much in our ICU despite of the high usage of urinary catheters (94.3% of ICU patients catheterised versus 75.2% and 95% in other studies)[16,24]. The CBD-device-use ratio was 0.79 making it below the 75th percentile of the NNIS (JUH = 0.75). The CBD-associated UTI rate was 2.9 patients per 1000 catheter days (<25th percentile of NNIS; JUH=15.57). Our low UTI rates were probably reflecting the strict aseptic technique of CBD insertion and close infection monitoring carried out in our ICU. Then again such differences could be due to under diagnosing UTI in these ICU patients. The diagnosis of UTI may be overlooked especially when common symptoms and signs of UTI such as dysuria, frequency, and suprapubic pain may be missed in the unconscious patient. We tended to have a higher suspicion of UTI when 'dirty' urine is seen in our patients.

As expected there were differences seen in mortality rates amongst the various studies. Such differences are also associated with the type of ICU as well as type of infection the patient is suffering from. The differences may also reflect differences in intensive care practice and patient selection rather than any real differences in absolute standards of care[15].

The EPIC study clearly showed significant correlation between the prevalence rate of ICU-acquired infections and the mortality rate (16.8%; ranging 8.4% to 28.5%, R^2=0.68). The risk of dying from a NI was highest when patients developed nosocomial pneumonia (13% to 55%)[19], laboratory-proven bloodstream bacteraemia and clinical sepsis (31% to 35%)[25]. In our series, the risk of dying from primary bacteraemia was higher then from nosocomial pneumonia (47.8% versus 41.2%). These rates quoted may be misleading, as patients may have more than one infection occurring at a time. As in our own study, the more sites of infection a patient had did not translate into a higher mortality rate; neither did it show any particular pattern in length of mechanical ventilation, duration of shock or ICU length of stay. It would have been better if in our study we were able to adjust these patients base on the degree of organ dysfunction or failure they had and see how this influenced the mortality rate, duration of ventilation, shock and ICU stay. It was unfortunate that the JUH and NNIS study did not have any figures on their ICU mortality rate.

The shortcoming of this study is the references used for comparison of data. The EPIC study is a 1-day point prevalence study, and as such only provides a snapshot in time, and in comparison with incidence studies, may actually overestimate a problem. The authors of the EPIC study further noted the possibility of selection bias regarding the identification and voluntary participation of the ICUs surveyed. However such bias may have been reduced by the fact that data acquisition was multidisciplinary.

In the NNIS study, the percentage of organism cultured was mainly hospital-wide rather than ICU specifically. As such the NNIS rates may be lower than those expected for an ICU. A comparison of organisms cultured from various institutions is important but mainly of academic rather than clinical interest. It is more important and clinically relevant to know your own hospitals or ICU organism profile. Further limitations in using the NNIS are the infrequency and unavailability of culturing in some of the participating hospitals.

It is further noted that information with regards to patients underlying and/or concomitant diseases, as well as their clinical status and ICU severity scores were not included in this study. Even though it is important for such information to be included especially when one is looking for a 'cause-effect' of nosocomial infection in ICU, the authors felt this was not in keeping with the main objective of this study looking at incidence of NI and as such was not included in the study.

Conclusion

ICU-acquired nosocomial infections are and still a major problem in ICUs. It results in increase ICU stay as well as extra costs attributable to infection[3,4,24]. This study has clearly documented the high incidence rate of ICU-acquired infection, and the importance of lower respiratory tract infection, pneumonia and bacteraemia in increasing ICU mortality. The need for vigilant surveillance as well as good infection control policy and management have shown in other studies to help reduce the incidence, cost and mortality of these groups of ICU patients[5]. In this study such conclusions could not be drawn, as data prior to the surveillance programme was not available for comparison. Nevertheless we did reduce the cost of unnecessary routine urine catheter tip and sample cultures (estimated saved cost of RM16, 000 per year), as these cultures are not done anymore in our ICU as part of the surveillance programme.

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