Microbial Isolates from Patients in an Intensive Care Unit, and Associated Risk Factors

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ABSTRACT

A retrospective one-year analysis of blood, sputum and urine samples taken from all patients admitted for more than 48 hours to the Intensive Care Unit at the University Hospital of the West Indies (UHWI) was undertaken. Positive trapped sputum cultures were found in 50% of patients, positive blood cultures in 32.7% and positive urine cultures in 23.1%. Gram-negative organisms predominated especially Pseudomonas aeruginosa *(41.3%) and* Acinetobacter spp *(33.5%). Coagulase-negative staphylococcus (20%) and streptococcus group D (18.7%) were the most common gram-positive organisms. The* Acinetobacter spp *showed marked resistance to most antibiotics except for meropenem (82.7% susceptibility) while* P aeruginosa *was most susceptible to ceftazidime (84.4%) and amikacin (89.1%). Both the coagulase-negative staphylococcus and streptococcus group D were relatively sensitive to amoxycillin/clavulanate (80.6% and 79.3% respectively). There was a high incidence of yeast found in sputum (27.1%) and urine (16.8%). Mechanical ventilation was a significant risk factor for developing a positive sputum culture ($p = 0.01$), this effect being particularly prominent in those ventilated for > 5 days. Central venous pressure lines significantly increased the risk of a positive blood culture ($p = 0.005$). This increase was seen particularly in those with CVP lines for > 7 days. Other risk factors for developing positive cultures included preadmission infection, antibiotic use just prior to ICU admission, increasing APACHE II score and increasing age.*

Aislados Microbianos de Pacientes en una Unidad de Cuidados Intensivos, y Factores de Riesgos Asociados

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RESUMEN

Un análisis retrospectivo de muestras de sangre, esputo y orina tomadas a todos los pacientes ingresados por más de 48 horas en la Unidad de Cuidados Intensivos del Hospital Universitario de West Indies (HUWI) fue realizado por espacio de un año. Se hallaron cultivos de esputo positivos en 50% de los pacientes, cultivos de sangre positivos en el 32.7%, y cultivos de orina positivos en el 23.1%. Hubo predominio de organismos gram-negativos, en especial Pseudomonas aeruginosa *(41.3%) y* Acinetobacter spp *(33.5%). Los estafilococos coagulasa-negativos (20%) y los estreptococos del grupo D (18.7%) fueron los organismos gram-positivos más comunes. Los* Acinetobacter spp *mostraron marcada resistencia a la mayoría de los antibióticos, salvo al meropenem (82.7% susceptibilidad), mientras* P aeruginosa *fue muy susceptible a la ceftazidima (84.4%) y a la amikacina (89.1%). Tanto el estafilococo coagulasa-negativo como el estreptococo del grupo D fueron relativamente sensibles a la amoxicilina/clavulanato (80.6% y 79.3% respectivamente). Se halló una alta incidencia de levadura en el esputo (27.1%) y la orina (16.8%). La ventilación mecánica fue un factor de riesgo importante para desarrollar un cultivo de esputo positivo ($p = 0.01$), siendo este efecto particularmente prominente en los ventilados por > 5 días. Las líneas de la presión venosa central aumentaron significativamente el riesgo de un cultivo de sangre positivo ($p = 0.005$), haciéndose este incremento particularmente evidente en aquellos con líneas de PVC por > 7 días. Otros factores de*

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riesgo para el desarrollo de cultivos positivos incluyeron las infecciones previas a la admisión, el uso de antibióticos justo antes del ingreso a la UCI, el aumento de la puntuación APACHE II cuenta, y la edad avanzada.

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INTRODUCTION

Infection rates in intensive care units (ICUs) have been documented to be the highest of all hospital acquired infections in large multicentre studies in the United States of America (USA) and Europe (1–3). Infection rates in the ICU range from 15% to 27% and are highest in surgical and burns ICUs and lowest in coronary care units (4). This is related to the use of large numbers of invasive monitoring devices, endotracheal and tracheostomy tubes; patient factors including extremes of age, immunocompromise state, malnutrition and severe underlying disease; and to a high incidence of cross infection (5, 6). These infections are costly to treat, prolong ICU stay and increase mortality rates (7). For example, in the USA, bloodstream infections have been shown to generate added costs of on average US$40 000 per survivor, to increase ICU stay by an average of eight days and to have an attributable mortality rate of 35% (8). Mortality rates as high as 40–80% have been observed in patients with nosocomial pneumonias (9).

The three most common nosocomial infections are ventilator-associated pneumonias, urinary tract infections and bloodstream infections (5, 10). In the European Prevalence of Infection in Intensive Care (EPIC) study done in 1992, pneumonia was the most common nosocomial infection (46.9%) followed by urinary tract infection (17.6%) and bloodstream infections (12%) (2). Data from the National Nosocomial Infection Surveillance System (NNIS) conducted between 1992 and 1997 from medical ICUs in the USA identified UTIs as the most frequent nosocomial infection (31%), followed by pneumonia (27%) and primary bloodstream infections (19%) (8). A one-day point-prevalence multicentre study conducted in Mexico in 1995 showed that the most frequently reported ICU-acquired infections were pneumonia (39.7%), urinary tract infections (20.5%), and bacteraemia (7.3%) (11). A report from Trinidad and Tobago conducted between 1998 and 1999 showed a 29.5% incidence of respiratory tract infections, a 20.1% rate of urinary tract infections and a 17.3% rate of bloodstream infections (12).

It is important to take steps to prevent ICU infections, but when they occur, effective and early institution of appropriate antibiotic therapy is crucial. This will improve patient outcome and decrease the incidence of multiple resistant organisms (13). The unique nature of the ICU environment makes this area of the hospital a focus for the emergence and spread of many antimicrobial-resistant pathogens (14). The Director General of the World Health Organization (WHO), in the WHO annual report on infectious diseases for 2000, notes that "if the world fails to mount a more serious effort to fight infectious diseases, antimicrobial resistance will increasingly threaten to send the world back to a pre-antibiotic age (15)."

There is wide diversity between institutions in the prevalence of pathogens and in their antimicrobial susceptibility. There is also variation in the frequency and types of infections among different subsets of patients within the same ICU (10,14). To produce effective empirical antibiotic protocols for individual ICUs, knowledge of common organisms and their sensitivity patterns is essential. The aim of this study was to determine the rate of positive cultures and to identify the common organisms and their susceptibility patterns from sputum, blood and urine samples of patients in the Intensive Care Unit, the University Hospital of the West Indies (UHWI) over a one-year period. Secondary goals included identifying significant risk factors for developing positive cultures and to assess the length of ICU admission and outcome of patients with positive cultures compared with those with negative cultures. The results of this study will help clinicians make the most rational choices of empiric antibiotic regimes based on common organisms, their antimicrobial susceptibility and the duration of invasive lines and mechanical ventilation.

METHODS

The UHWI, Kingston, Jamaica, has an eight-bed general intensive care unit that accepts surgical, medical, paediatric, obstetric and gynaecological patients. The hospital has a separate neonatal ICU (NICU), but occasionally, neonates are admitted to the general ICU when the NICU is full. A retrospective analysis of the medical data of all patients admitted to the general ICU, UHWI, between January 1, 2001 and December 31, 2001, was undertaken. Patients who were discharged or died within 48 hours of admission were excluded from the study group. All cultures of sputum, urine and blood taken during the study period were analyzed. Sputum and urine cultures were routinely performed on all ventilated and catheterized patients twice weekly. Blood cultures were done in febrile patients (temperature $ 38° C) with leucocytosis (WBC $ 11 x 10^6/L) and those with prolonged central venous pressure (CVP) catheterization (> 5 days). Positive cultures obtained prior to admission or within the first 48 hours of admission were recorded as pre-existing infections.

A positive culture was defined as identification of organisms on gram stain followed by growth of the organism in the appropriate culture medium. In blood and sputum cultures, any growth obtained was reported. All positive isolates were included in the study and no inference based on the

Q-score or its variants were made. Clinical criteria (pyrexia, purulent tracheal aspirate, chest radiograph findings) were also not used for screening the samples. Quantitative examination was done on the routine urine cultures to exclude normal flora and contaminants, and the presence of more than 10^5 bacteria of the same type /ml of urine signified a urinary tract infection. Growth of $ 4 organisms was reported as a contaminated sample. All urine samples were cultured, even if the urinalysis was negative.

Antibiotic susceptibility was tested by the Kirby Bauer single disk diffusion technique on DST agar. Antibiotics tested and the concentrations used were: amoxicillin-clavulanic acid 30µcg, methicillin 5µcg, ceftazidime 30µcg, ceftriaxone 30µcg, trimethoprim-sulphamethoxazole 25µcg, gentamicin 10µcg, amikacin 30µcg, ciprofloxacin 5µcg and meropenem 10µcg. National Committee for Clinical Laboratory Standards (NCCLS) guidelines were used to interpret the results obtained. Three control strains from the American Type Culture Collection (ATCC) were used to ensure the quality of testing: *Escherichia coli* ATCC 25922, *Pseudomonas aeruginosa* ATCC 27853 and *Staphylococcus aureus* ATCC 25923.

Other data collected for each patient included age, gender, underlying/chronic disease, APACHE II score, referring specialty, presence of any preadmission infection, pre-existing use of antibiotics, patient outcome (died or discharged) and length of ICU admission. The use of mechanical ventilation and/ or invasive lines and their duration of use were documented.

Statistical analysis was done using the Statistical Package for the Social Sciences (SPSS, Chicago, II) Version 10. The occurrence of positive cultures, and correlation of various patient factors with contracting a nosocomial infection were assessed. The chi-square test was used to test for statistical significance of categorical variables and was set at a *p*-value < 0.05. Multivariate analyses with logistic regression models were carried out to assess for independent risk factors for the presence of infection.

RESULTS

One hundred and fifty-five patients were enrolled in the study. Their ages ranged from one day to 94 years, with a mean of 44.0 years (Fig.1). There were 80 males and 75 females. Ninety-nine patients (63.9%) were admitted under the care of a surgical service. Thirty-five patients were medical (22.6%), 13 were paediatric (8.4%) and 8 were obstetric/-gynaecological (5.2%). A positive sputum culture was found in 50% (78/155) of the patients, a positive blood culture in 32.9% (51/155) and a positive urine culture in 23.9% (37/155). Sixty-six patients (42.6%) had negative cultures and 53 patients (34.2%) had multiple sites positive. Positive sputum cultures were monomicrobial in 65.6% of cases, grew two organisms in 30.2% and three or more organisms in 4.2%. For positive blood cultures, 57.6% grew one organism, 40.7% grew two organisms and 1.7% grew three organisms. Approximately half of the positive urine cultures were mono-microbial (54.8%).

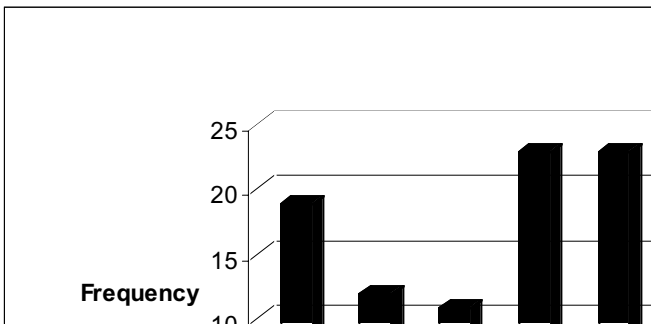

Fig. 1: Distribution of ages of patients admitted to the ICU, UHWI, 2001.

The rank order of pathogens cultured from sputum was yeast (27.1%), *Pseudomonas aeruginosa* (23.2%), *Acinetobacter* spp (23.2%), coagulase-negative *staphylococcus* (10.3%), *Enterobacter cloacae* (7.7%), *Streptococcus* group D (7.1%) and *Stenotrophomonas maltophilia* (6.5%). Other organisms included *Streptococcus viridans* (5.8%), *Alkaligenes* (3.2%), *Serratia* (3.2%), *Klebsiella pneumoniae* (2.6%) and *E coli* (0.6%) (Fig. 2). The organisms cultured

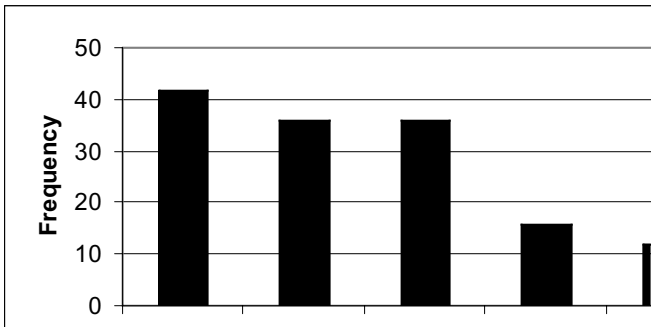

Fig. 2: Organisms cultured from sputum samples of patients in the ICU, UHWI, 2001

* CNS = Coagulase-negative *staphylococcus*
** Other = *Streptococcus viridans, Staphylococcus aureus, Alkaligenes sp, Serratia sp, Klebsiella pneumoniae, E coli*

from blood in decreasing frequency were *Pseudomonas aeruginosa* (14.2%), *Acinetobacter* spp (7.7%), coagulase negative *staphylococcus* (7.1%), *Enterobacter cloacae* (7.1%), *Stenotrophomonas maltophilia* (6.5%) and *Streptococcus* Group D (5.8%). Other organisms included *Alkaligenes* spp (4.5%), *Klebsiella pneumoniae* (1.9%) and yeast (0.6%) (Fig. 3). Organisms grown from urine cultures included yeast (16.8%), *Streptococcus* group D (5.8%), *Pseudomonas aeruginosa* (3.9%), *Acinetobacter* spp (2.6%), coagulase negative *staphylococcus* (2.6%) and *E coli* (2.6%) (Fig. 4).

The majority of the organisms cultured from all three sites in this study were gram-negative bacilli; most commonly *Pseudomonas aeruginosa* (41.3%) and *Acinetobacter* species (33.5%). Coagulase negative

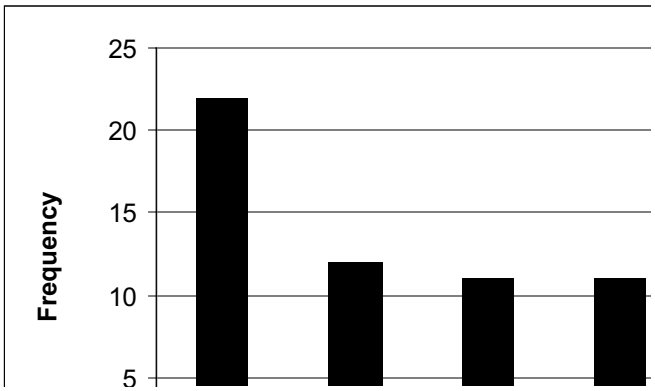

Fig. 3: Organisms cultured from blood samples of patients in the ICU, UHWI, 2001

*CNS = Coagulase-negative *staphylococcus*
**Other = *Klebsiella pneumoniae,* microaerophilic *streptococcus*, *Staphylococcus aureus*, yeast, *Streptococcus pneumoniae, Proteus*

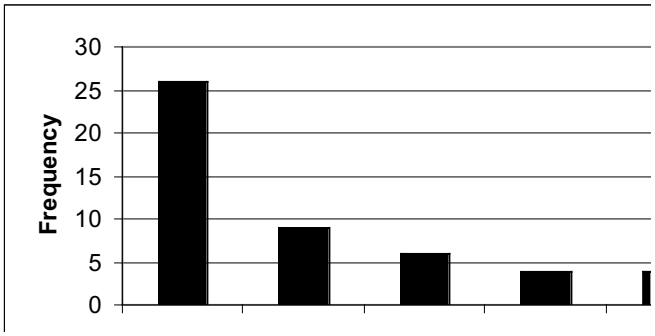

Fig. 4: Organisms cultured from urine samples of patients in the ICU, UHWI, 2001

*CNS= Coagulase-negative *staphylococcus*
** Other = *Klebsiella pneumoniae, Enterobacter sp*, *Streptococcus* group B.

staphylococcus (20%) and *Streptococcus* Group D (18.7%) were the most common gram-positive organisms. The antibiotic sensitivity patterns for the most common organisms cultured are shown in Table 1. The most effective antibiotics against the *P aeruginosa* were ceftazidime and amikacin (84.4% and 89.1% susceptibility rates respectively). The *Acinetobacter* was remarkably resistant to most antibiotics except meropenem (82.7% susceptible). The coagulase negative *staphyloccus* was sensitive to amoxycillin/clavulanate (80.6%). *Streptococcus* Group D responded reasonably well to amoxycillin/clavulanate (79.3% susceptibility).

Effect of Mechanical Ventilation and Invasive Lines

Mechanical ventilation was a significant risk factor for a positive sputum culture. Patients who were ventilated had a 52.7% occurrence of a positive sputum culture compared with 18.8% in those who were not ventilated ($p = 0.01$). Positive cultures became more prominent after five days of mechanical ventilation. Patients who were ventilated for # 5 days had a 20.0% occurrence of a positive sputum culture compared with 80.3% in those ventilated for six or more days. The organisms cultured differed between the early onset (# 5 days) and late onset (> 5 days) cultures. Yeast and *P aeruginosa* predominated in the former whereas *Acinetobacter spp* became more prevalent in the latter (Table 2).

Patients with central venous pressure (CVP) lines were more likely than others to have a positive blood culture. A 38.0% frequency was seen in patients with CVP lines compared with an 8.3% incidence in those without CVP lines ($p = 0.005$). Patients with CVP lines for greater than seven days were more likely to have a positive blood culture (52.3%) than those with lines for seven days or less (18.0%).

None of the patients without urethral catheters had a positive urine culture compared with 25% of patients who

Table 1: Antibiotic profile of organisms isolated from blood, sputum and urine of patients admitted to the ICU of the UHWI, 2001

		Antibiotic								
Organism	**n**	Aug n (%)	Meth/ Clox n (%)	Ceftaz n (%)	Ceftriax n (%)	Genta (%)	Amik n (%)	Cotrim n (%)	Cipron n (%)	Mero n (%)
Gram-negative										
P aeruginosa	64	NT	NT	54 (84.4)	2 (3.1)	49 (76.6)	57 (89.1)	NT	35 (54.7)	NT
Acinetobacter	52	7 (13.5)	NT	15 (28.8)	8 (15.4)	11 (21.2)	32 (61.5)	12 (23.1)	13 (25.0)	43 (82.7)
E cloacae	24	1 (4.2)	NT	13 (54.2)	13 (54.2)	18 (75.0)	13 (54.2)	17 (70.8)	8 (33.3)	18 (75.0)
S maltophilia	20	1 (5.0)	NT	15 (75.0)	NT	0	0	20 (100)	18 (90.0)	9 (45.0)
Alkaligenes spp	12	7 (58.3)	NT	7 (58.3)	5 (41.7)	1 (8.3)	5 (41.7)	5 (41.7)	5 (41.7)	11 (91.7)
K pneumoniae	8	7 (87.5)	NT	5 (62.5)	4 (50.0)	8 (100)	8 (100)	5 (62.5)	8 (100)	8 (100)
Escherichia coli	5	3 (60.0)	NT	NT	NT	4 (80.0)	NT	5 (100)	NT	NT
Gram-positive										
CN staph	31	25 (80.6)	15 (48.4)	NT	NT	6 (19.4)	NT	NT	NT	NT
Strep Gp D	29	23 (79.3)	NT	NT	NT	1 (3.4)	NT	6 (20.7)	NT	NT

Legend: Aug = amoxycillin/clavulanate; Meth/Clox = methicillin/ cloxacillin; Ceftaz = ceftazidime; Ceftriax = ceftriaxone; Genta = gentamicin; Amik = amikacin; Cotrim = cotrimoxazole; Cipro = ciprofloxacin; Mero = meropenem; NT = not tested
CN staph = coagulase negative staphylococcus

Table 2: Common organisms cultured from sputum, according to duration of mechanical ventilation – ICU, UHWI, 2001

Organism	No positive sputum cultures	(%)
Mechanical ventilation # 5 days (n = 48)		
Yeast	20	(41.7)
Pseudomonas aeruginosa	12	(25.0)
Acinetobacter	6	(12.5)
Coagulase-negative *staphylococcus*	5	(10.4)
Streptococcus viridans	5	(10.4)
Mechanical ventilation > 5 days (n = 106)		
Acinetobacter	30	(28.3)
Pseudomonas aeruginosa	24	(22.6)
Yeast	22	(20.8)
Coagulase-negative *staphylococcus*	11	(10.4)
Streptococcus group D	10	(9.4)
Stenotrophomonas maltophilia	9	(8.5)

were so catheterized. This difference did not achieve statistical significance (p = 0.13).

Effect of Patient Factors

There was an increase in occurrence of positive cultures in patients > 70 years old (79.3% compared with 53.6% in those less than 70 years old) (Table 3) but this did not achieve statistical significance (p = 0.35). Neither gender nor the presence of diabetes mellitus had any statistically significant effect on the frequency of positive cultures (p = 0.14 and 0.81 respectively). Pre-admission infection and antibiotic use significantly increased the risk of positive cultures (p = 0.002 and 0.001 respectively). All except one patient had an APACHE II score of between 1 and 39 (worsening score represents increasing severity of illness, maximum = 71). There was a significant increase in positive cultures with an increasing APACHE II score (p = 0.02) (Table 3).

Table 3: Culture results as a function of patient factors, ICU, UHWI 2001

Factor	Culture result		No data	p-value
	Negative (%)	Positive (%)		
Gender				
Male	29 (36.3)	51 (63.8)		
Female	36 (48.0)	39 (52.0)	0	0.14
Age				
< 70 years	58 (46.4)	67 (53.6)		
> 70 years	6 (20.7)	23 (79.3)	1	0.35
Diabetes mellitus				
No	57 (42.9)	76 (57.1)		
Yes	8 (40.0)	12 (60.0)	2	0.81
APACHE II score				
0–9	15 (71.4)	6 (28.6)		
10–19	25 (45.4)	30 (54.5)		
20–29	9 (27.3)	24 (72.7)		
30–39	2 (33.3)	4 (66.7)		
$ 40	1 (100)	0	39	0.02*
Pre-admission infection				
No	53 (53.0)	47 (47.0)		
Yes	11 (22.9)	37 (77.1)		
Presumed	1 (33.3)	2 (66.7)	4	0.002*
Prior use of antibiotics				
No	52 (52.5)	47 (47.5)		
Yes	13 (25.0)	39 (75.0)	4	0.001*

* statistically significant

Stepwise logistic regression models were used to remove the effects of confounding variables. Age and pre-admission infection were the independent factors found to significantly affect obtaining a positive culture (p = 0.03 and 0.001 respectively).

Effect of Positive Cultures on Patient Outcome

The mortality rate of patients with positive cultures was 30.0% compared with 23.1% in those with negative cultures. This difference was not statistically significant (p = 0.33). Patients who had a positive culture from any specimen (or multiple specimens) spent a mean of 16.9 ± 14.6 days in ICU compared with 5.1 ± 4.7 days for those patients with negative cultures (p = 0.001).

DISCUSSION

While positive blood cultures will reflect a septicaemia unless contamination occurred, positive trapped sputum and urine cultures will represent a combination of true nosocomial infections as well as colonization of the upper airway (with trapped sputum samples) or the lower urinary tract (with urine samples). Colonization refers to the presence of micro-organisms on mucosal surfaces of the body without invasion of cells or stimulation of an inflammatory response. A nosocomial infection is usually diagnosed on the basis of positive cultures in the presence of one or more of the following clinical findings: *pyrexia* ($ 38° C) or *hypothermia* (# 36° C), increased white cell count, and additionally for VAP only, purulent tracheal aspirate, chest signs on auscultation and new infiltrates on chest radiograph (7). Even when this combination of signs is used, nosocomial infections, especially VAPs, are frequently overdiagnosed. More invasive tests such as bronchoalveolar lavage (BAL), or protected brush specimens (PBS) may be done, but these involve greater expense and expertise and are not practicable for many developing countries (9). The microbials present in sputum and urine are the same organisms that may produce a florid VAP or UTI at a later date, so the results from trapped sputum and urine cultures will accurately reflect nosocomial infections in the ICU. The incidence of positive cultures will, however, be higher than those reported for nosocomial infections.

As expected, the occurrence of positive sputum cultures (50%) and urine cultures (23.1%) in this study were higher than those reported in other studies (2, 8, 11–12). However, the frequency of positive blood cultures (32.7%) was much higher than reported elsewhere (8, 11–12). This

could represent contaminated samples and stricter inclusion criteria in other studies that used definitions including clinical signs as well as a positive blood culture. In addition, questions could be raised about the use of CVP lines and guidelines relating to their placement, use and removal may be necessary.

A large number of sputum and urine cultures grew yeast, which may be due in part to the immunocompromised state of many of the patients (as a result of, for example, poor nutritional state, diabetes mellitus and steroid use) and the use of broad-spectrum antibiotics. This may, however, also indicate an overuse of antibiotics and the need for stricter control measures, especially as positive yeast cultures were commoner during the earlier stages of admission (10, 11). The quandary is whether these infections should be treated with antifungal agents. If yeast is isolated from a blood culture, treatment should be started and the CVP line removed. Yeast cultured from urine in the asymptomatic patient may be due to catheter colonization. The catheter should be changed and the culture repeated. If the second culture is also positive, or the patient is unstable, neutropenic or a transplant recipient, a blood culture should be done and treatment commenced. Yeast grown from sputum is also usually due to colonization, and treatment is only commenced in severely ill, neutropenic or immunocompromised patients (16).

This study suggests that early empiric antibiotic therapy in the ICU at the UHWI should include meropenem and/or ceftazidime or amikacin to cover for *Acinetobacter* and *P aeruginosa*. Combination therapy for *P aeruginosa* has been shown to decrease hospital mortality rate when compared to monotherapy (16). Patients with prolonged mechanical ventilation should also be covered with trimethoprim-sulphamethoxazole or ciprofloxacin for *S maltophilia*. If a gram-positive organism is seen on the initial gram stain, amoxycillin/clavulanate should be used until sensitivity patterns become available. We need to explore sensitivity patterns to other agents less commonly used, such as piperacillin/tazobactam. Antifungals should also be considered in patients not responding to broad-spectrum antibiotics and who are severely immunocompromised, as evidenced by the high occurrence of positive yeast cultures.

The results of this study clearly indicate that the most susceptible patients to nosocomial infection are the elderly, those with previous infections or previous antibiotic therapy and the most severely ill (increasing APACHE II scores) (17). Prolonged mechanical ventilation (> 5 days) and prolonged CVP catheterization (> 7 days) were also associated with significantly increased risk of positive cultures. These results are not surprising because both the endotracheal tube and CVP line act as portals of entry for pathogens. Similar results have been reported in a number of other studies (7, 11).

Mortality rates were not significantly different between patients with and without positive cultures, unlike several other studies (2, 7–9). This discrepancy highlights the fact that not all patients with positive cultures had an active nosocomial infection. The hospital stay of patients with positive cultures averaged an additional 11 days, leading to greatly increased costs and possible increased morbidity.

In summary, nosocomial infections continue to be a major problem in the ICU, UHWI, and have been shown to increase patient morbidity. The results of this study emphasize the importance of local surveillance programmes to correctly guide empiric therapy. Strategies to control these infections must therefore include knowledge of infection rates, common pathogens, their antibiograms and risk factors for acquiring these infections. This will assist clinicians in choosing appropriate empiric antibiotics to maximize the patients' chances of receiving early and effective therapy. Surveillance must be ongoing, however, to reflect changes in microbial flora and to review regularly antibiotic protocols to keep clinicians current.

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