

Spectrum of microbial growth and antimicrobial usage in an intensive-care unit of a tertiary-care hospital in Trinidad, West Indies

S Bidaisee, MBBS, DM; S Hariharan, MBBS, MD, PhD, FCCM; D Chen, MBBS, FRCA, MBA

Anaesthesia and Intensive Care Unit, Faculty of Medical Sciences, University of the West Indies, St. Augustine, Trinidad and Tobago

Corresponding author: S Hariharan (uwi.hariharan@gmail.com)

Background. Intensive-care units (ICUs) are a source of multidrug-resistant organisms, owing to the indiscriminate usage of broad-spectrum antimicrobial drugs. In such settings, one must be aware of the spectrum of microbes and pattern of antibiotic usage.

Objectives. To evaluate the spectrum, susceptibility and resistance patterns of microbes found in ICU patients in a tertiary-care teaching hospital in Trinidad, and to quantify antimicrobial usage.

Methods. All adult patients (≥ 15 years of age) admitted to the ICU for ≥ 48 h who developed nosocomial infections conforming to the Centers for Disease Control and Prevention criteria were included. Demographic data and clinical data, including specimens sent, isolates grown, antimicrobial sensitivity and resistance patterns, the usage of antimicrobials and patient outcomes, were recorded. Variables such as age, admission white blood cell count, duration of first antibiotic used, length of ICU stay, length of hospital stay, organ support and total comorbidities were analysed. Antimicrobial usage was quantified as the defined daily dosage per 1 000 patient-days.

Results. A total of 153 patients with 287 microbiological specimens were studied. The mean patient age was 48.4 years, and the mean ICU length of stay was 7.9 days. The most common admitting diagnoses were sepsis and multiple trauma. *Staphylococcus aureus* was the most common isolate from blood and central venous lines, and *Pseudomonas aeruginosa* from tracheal aspirates and wound swabs. Non-survivors had significantly higher age, leucocyte count and organ support requirements, and shorter lengths of stay. Cefuroxime was the most-used antimicrobial in the unit.

Conclusion. The usage pattern of antimicrobials did not correlate with susceptibility in most instances. There is a need to improve antimicrobial usage by implementing antimicrobial-stewardship programmes to establish an antimicrobial protocol and guidelines for usage in the ICU.

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Hospital-acquired infections (HAIs) are a major cause of morbidity and mortality in patients admitted to hospitals, and can lead to the spread of multidrug-resistant pathogens.^[1] HAIs, by definition, may be either local and/or systemic, and result from the presence of an infectious agent or its toxin after 48 hours or more following a hospital admission, where the incubation period for the infection does not occur prior to hospital admission.^[2] Over the years, patterns of microbial growth have seen many shifts, with emerging strains of potential drug-resistant species, including methicillin-resistant *Staphylococcus aureus* (MRSA), *Pseudomonas* spp., *Acinetobacter* spp., *Stenotrophomonas maltophilia* and extended-spectrum beta-lactamase (ESBL)-producing Gram-negative organisms.^[3]

Inappropriate antimicrobial use and poor prescription practices have contributed to the development of multidrug-resistant organisms, rendering treatment of HAIs very difficult.^[4] In addition, failure to comply with infection-control measures has a negative impact on hospital infection rates. Overcrowding and understaffing of wards also contribute to HAIs in the developing world. In low- and middle-income countries, the major factors contributing to serious nosocomial infections include lack of infrastructure, inconsistent surveillance, deficiency in trained personnel and infection-control programmes, and poverty-related factors.^[5]

Intensive-care patients are often the most susceptible to HAIs, due to the acute disease process, the presence of comorbidities, invasive devices,

exposure to various procedures and general immunocompromised status.^[6] Therefore microbial surveillance and knowledge of resistance patterns to antimicrobials is critically important in any ICU setting. A recent review showed that the implementation of continuous surveillance measures had a positive impact in controlling nosocomial infections.^[7] Although surveillance programmes may be relatively expensive to implement, they are indeed cost-effective when compared to the expenditure of treating sepsis and the morbidity associated with it. Surveillance studies also play a vital part in the optimal management of infections in the intensive-care setting. Many developed countries have well-established surveillance teams and programmes that have accounted for lower infection rates when compared with less-developed countries.^[8] In the USA, the Centers for Disease Control and Prevention (CDC) launched a subset division called the National Nosocomial Infections Surveillance System in 2004, and publish yearly benchmarks for the surveillance measures.^[9] Such surveillance, along with intervention with prevention strategies, can decrease infection rates, morbidity and mortality, increasing patient safety.

The International Nosocomial Infection Control Consortium is an international collaborative body founded 10 years ago to promote infection control in the hospitals of countries with limited resources.^[10] Thus far, it has been successful in increasing compliance rates for prevention strategies and has reduced the rates of HAI.^[11] Trinidad and Tobago, unfortunately, has not been part of any such international programme.

Against this background, this study aimed to look at the microbial growth patterns, susceptibility profiles, resistance patterns and antimicrobial usage in the ICU at Eric Williams Medical Sciences Complex, a major tertiary-care teaching health facility in Trinidad.

Design and methods

Study setting

Trinidad is one half of the twin island-nation of Trinidad and Tobago, with a population of approximately 1.3 million. The study hospital has 323 beds and the Intensive Care Unit (ICU) is a 10-bed mixed surgical and medical ICU. Admissions to the ICU are either directly from the emergency departments, the operating theatres, the High Dependency Unit or the general wards. The ICU team consists of an anaesthesia consultant, a registrar and two house officers. Although the aim is to have a nurse-to-patient ratio of 1:1, sometimes it happens to be 1:2. Four beds are in isolation rooms at the back of the ICU, and are designated for barrier nursing. An infection prevention and control officer visits the ICU on a daily basis.

Description of the study

Approval for this retrospective observational study was obtained from the Ethics Committee of the Faculty of Medical Sciences, University of the West Indies, with a waiver of individual informed patient consent. Approval was also given by the medical chief of staff and the head microbiologist at the hospital.

All adult patients (≥ 15 years of age) admitted to the ICU between January 2008 and June 2010 for ≥ 48 h who developed nosocomial infections meeting the CDC criteria were included. Paediatric patients (i.e. < 15 years) and patients admitted for < 24 h were excluded.

Data collection

The demographic data on patient age and gender were collected. The clinical data collected included the following:

- admission diagnosis
- comorbidities
- body temperature on admission
- leukocyte count on admission
- culture sites/specimens sent
- isolates grown from specimens
- sensitivity profiles and resistance patterns for each isolate
- antimicrobial agent(s) used in each patient throughout the stay, including the dosage and duration of use
- length of stay in ICU and hospital
- types of organ support provided in the ICU – mechanical ventilation for the respiratory system, renal-replacement therapy for acute kidney injury, haemodynamic support (pharmacological/intra-aortic balloon pump, etc.) for the cardiovascular system.
- patient outcome – death or discharge from ICU.

In this hospital, during the study period, the ICU did not have a surveillance policy. Specimens were taken from patients based on clinical requirements as ordered by the intensivists. In addition, the microbiology laboratory did not have an international policy manual to follow. The testing was done based on guidelines proposed by the consultant microbiologist, which were based on those recommended by the American Society for Microbiology. The study samples were processed as follows:

As per hospital general procedure, blood-culture samples taken on wards are placed in either aerobic or anaerobic bottles. In the laboratory,

these samples are placed in a Bactec 9240 (BD, USA) machine set at 35°C, where they are rotated. Once CO₂ is detected by the machines, the bottles are removed and set for Gram stain and plating. The samples are plated on different media (blood, chocolate agar, MacConkey agar, anaerobic agar). Each medium is set at specific temperatures and left for 5 days to observe for growth, but they are monitored on a 24-hour basis.

Catheter tips (e.g. central venous catheter (CVC) tips) are rubbed onto the plates and streaked. Any wet material present on the catheter is also Gram stained. Urine samples obtained are either catheter or midstream samples, and either they are placed in a calibrated loop, or the appropriate quantity of urine is placed on a cystine lactose electrolyte deficient (CLED) plate to observe for growth. Tracheal aspirates are obtained from suctioning of a patient's trachea with inline suction traps. In the laboratory, they are plated on blood, or MacConkey or chocolate agar. The isolates are then tested for antimicrobial susceptibility using disks which have been incubated overnight, and the minimum inhibitory concentration is estimated in accordance with the standards of the Clinical and Laboratory Standards Institute.

Data analysis

Data were entered into Excel spreadsheets and Statistical Package for Social Sciences (SPSS) version 12 (IBM, USA) was used for statistical analyses. Statistical significance was fixed at $p < 0.05$. Descriptive analyses were used for demographic data, and independent *t*-tests were used to compare the variables such as age, admission white blood cell count (WBC), duration of first antibiotic used, length of ICU stay, length of hospital stay, organ support and total comorbidities between patients who died in the ICU and those who survived.

Antimicrobial usage was represented as defined daily dosage (DDD) per 1 000 patient-days (using the following formula:

$$\text{DDD} = \frac{\text{DDD for specific agent (ATC/DDD Code)}}{\text{Total number of patient-days}} \times 1\,000$$

Results

A total of 153 patients were included in the study, 79 (51.6%) of whom were female. The most common admitting diagnoses were multiple trauma and neurological disorders, and the most common comorbidities were diabetes mellitus, hypertension and ischaemic heart disease. Fig. 1 depicts the distribution of the diagnoses on admission to ICU.

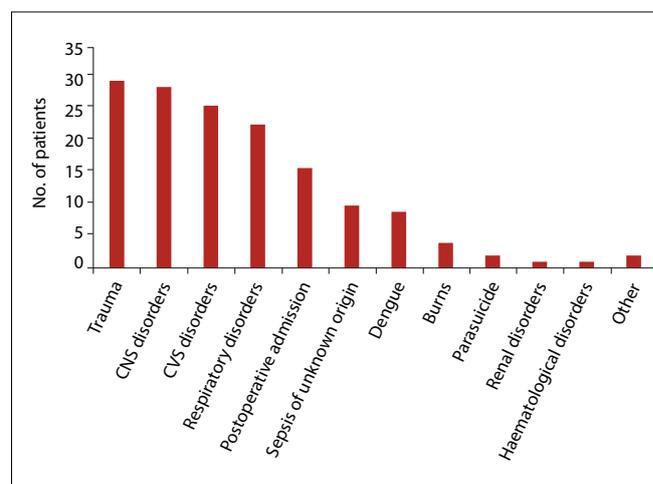


Fig. 1. Distribution of diagnoses on admission. (CNS = central nervous system; CVS = cardiovascular system.)

The age of patients ranged from 16 to 90 years. The mean (standard deviation (SD)) age of patients was 48.4 (18.7) years (range 16 - 90) and the mean (SD) WBC on admission was 12.9 (5.9) (range 4.2 - 40.9). The mean (SD) length of ICU stay was 7.9 (5.9) (range 2 - 33) days, while the mean (SD) overall length of hospital stay was 15.3 (9.7) (range 2 - 65) days.

The comparison between patients who survived their ICU stay and those who died is shown in Table 1. The length of ICU stay and duration of first antibiotic use did not show a statistically significant difference between the two groups. With respect to age, the survivors were younger than those who died ($p=0.01$). The non-survivors had a higher WBC count on admission when compared with those who survived ($p=0.02$). As expected, the patients who had a higher number of comorbidities and required more organ support had a higher mortality ($p<0.001$).

Of all the patients, only two did not require organ support, and were admitted for close monitoring of vital signs. The majority (62.7%) of patients received support for one organ in the form of mechanical ventilation and 33.3% received support for two organs. The most common (96.7%) organ system supported was the respiratory system. Of these, 3 patients (1.9%) required non-invasive positive-pressure ventilation, while the remainder required invasive ventilation. Inotropic support was required in 52 patients (33.9%), while 3 patients (1.9%) needed renal replacement therapy (RRT). While 107 patients (69.9%) were discharged from the ICU, 46 (30.1%) died.

In total, 88 patients had at least one isolate in one of the specimens sent to the microbiology laboratory, meaning that the prevalence rate of nosocomial infections in this ICU was 57.5%. The total number of specimen samples sent for microbiological analysis during the study was 282. The various specimens included blood, tracheal aspirates, urine, CVC tips, wound swabs, urinary catheter tips and pleural fluid. Wound

swabs had the highest prevalence of microbial growth (95%), followed by tracheal aspirates (78%). Blood was the most common sample site to be cultured, accounting for 105 specimens (36.6%).

The isolates grown from the different specimens are shown in Table 2. In general, *Pseudomonas aeruginosa* and *Enterobacter* spp. were reported in all the various sites and specimens sampled for microbiological analyses, while *Staphylococcus aureus* was reported in all except urine.

P. aeruginosa was predominantly sensitive to gentamicin (63.1%), as well as to ciprofloxacin (60.1%). It showed 37% sensitivity to piperacillin/tazobactam. Sensitivity to imipenem was 32% while meropenem was at 13%. It was least sensitive to ceftazidime (8%). Fig. 2 shows the individual sensitivity and resistance pattern of this organism. Fig. 3 shows the sensitivity profile for *Klebsiella*, and of particular note is that 5% of these isolates were resistant to meropenem.

Fig. 4 shows the sensitivity-resistance pattern of *S. aureus*. A total of 42% of these isolates were sensitive to oxacillin, amoxicillin/lavulanic acid and gentamicin.

S. epidermidis showed highest sensitivity to gentamicin, followed by levofloxacin. Sensitivity to cefuroxime was 19%, while that for cefotaxime was 3%. Resistance to gentamicin was at 19%, while that for piperacillin/tazobactam and imipenem was 6% each.

Enterobacter spp. showed 75% sensitivity to gentamicin. Sensitivity to ciprofloxacin was at 60% and piperacillin/tazobactam at 50%. Sensitivity to cefotaxime and ceftazidime were at 5% each. Resistance was highest for ciprofloxacin and lowest for gentamicin at 5%.

S. haemolyticus showed no resistance to the cephalosporins, gentamicin or vancomycin.

Methicillin-resistant *S. aureus* was sensitive to linezolid (71%), tigecycline (57%) and rifampin (43%). There was no vancomycin-resistant specimen in this study.

Table 1. Comparison of patient variables between survivors and non-survivors

Variable	Overall, mean (SD)	Survivors, mean (SD)	Non-survivors, mean (SD)	<i>p</i> -value*
Age (years)	48.4 (18.7)	45.7 (18.3)	54.7 (18.4)	0.01
Admission leukocyte count ($\times 10^3/\mu\text{L}$)	13.0 (5.9)	12.3 (4.9)	14.6 (7.4)	0.02
Hospital length of stay (days)	15.3 (9.7)	16.9 (9.8)	11.8 (8.7)	0.002
Organ support (<i>n</i>)	1.3 (0.5)	1.2 (0.5)	1.7 (0.6)	<0.001
Total comorbidities (<i>n</i>)	1.57 (0.8)	1.48 (0.8)	1.78 (0.8)	0.04
Duration of first antibiotic (days)	6.9 (3.9)	6.9 (3.6)	6.8 (4.6)	0.855

*Statistical significance by independent *t*-test.

Table 2. Isolates from various specimens

Organisms identified	Blood (N=105)	Tracheal aspirate (N=94)	Urine (N=43)	CVC (N=20)	Wound swabs (N=20)
Total isolates	51	73	13	14	19
Sterile (no bacterial growth)	54 (51.6)	21 (22.3)	30 (69.8)	6 (30.0)	1 (5.0)
<i>Pseudomonas aeruginosa</i>	4 (7.8)	24 (32.8)	1 (7.7)	2 (14.3)	8 (42.1)
<i>Staphylococcus aureus</i>	7 (13.7)	4 (5.5)	2 (15.4)	-	2 (10.5)
<i>S. haemolyticus</i>	8 (15.6)	1 (1.3)	-	1 (7.1)	-
<i>S. epidermidis</i>	23 (45.1)	1 (1.3)	1 (7.7)	8 (57.1)*	-
<i>Enterobacter</i> spp.	4 (7.8)	11 (15.1)	2 (15.4)	1 (7.1)	1 (5.2)
<i>Klebsiella</i>	5 (9.8)	13 (16.7)	2 (15.4)	-	2 (10.5)
MRSA	-	5 (6.8)	-	1 (7.1)	3 (15.8)
<i>Candida</i> spp.	-	1 (1.3)	4 (30.8)	-	-
Other	-	13 (17.8) [†]	-	1 (7.1) [‡]	3 (15.8) [§]

CVC = central venous catheter; MRSA = methicillin-resistant *Staphylococcus aureus*.

*One isolate was MRSA.

[†]*S. maltophilia*, *S. pneumoniae*, *S. viridans*, *Moraxella*, *Acinetobacter*.

[‡]*Serratia*.

[§]*Serratia*, *Citrobacter*, *Acinetobacter*.

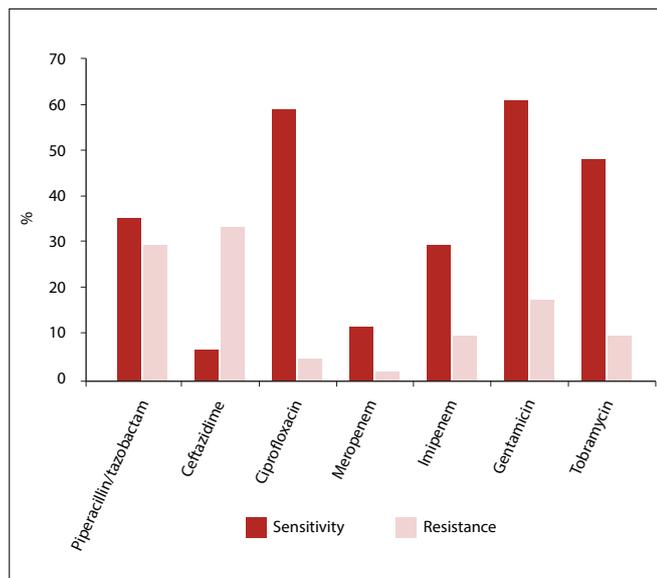


Fig. 2. Sensitivity-resistance patterns for *Pseudomonas aeruginosa*.

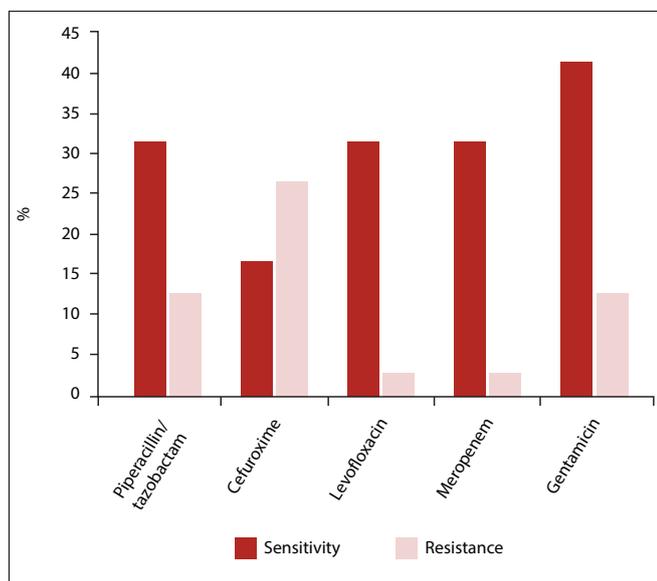


Fig. 3. Sensitivity-resistance patterns for *Klebsiella*.

Acinetobacter showed high sensitivity to piperacillin/tazobactam, ceftazidime, imipenem and tobramycin, gentamicin and levofloxacin; however, only 20% each of the isolates showed sensitivity to meropenem and ceftazidime.

S. maltophilia was isolated in two blood specimens. On both occasions it was sensitive to gentamicin (100%), but only once to amikacin and levofloxacin (50% each). There was 100% resistance to tobramycin.

The antimicrobial usage during the study period is depicted in Table 3 as the DDD per 1 000 patient-days, along with the respective anatomical therapeutic chemical (ATC) classification and DDD code. The most common antibiotic prescribed in this study group was cefuroxime. Piperacillin/tazobactam, meropenem and ceftriaxone were the second, third and fourth most commonly used antimicrobials, respectively.

Antibiotic usage ranged from one agent to a maximum of four agents per patient throughout ICU stay, and the ranges of duration of antibiotic use are shown in Table 4. Monotherapy was used in 51 patients (33.1%), while 57 patients (37.3%) were given two antibiotics. Three antibiotics

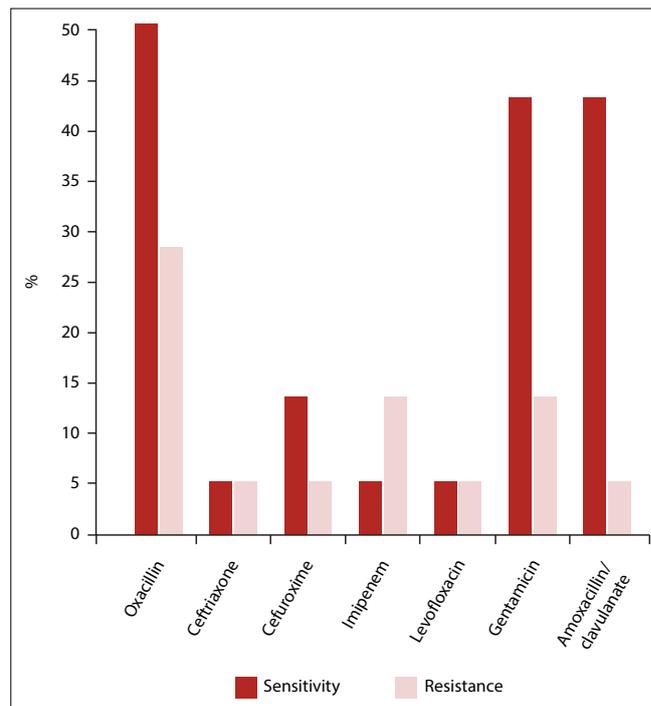


Fig. 4. Sensitivity-resistance patterns for *Staphylococcus aureus*.

Table 3. Antimicrobial usage as DDD per 1 000 patient-days

Antimicrobial	ATC/DDD code	DDD
Cefuroxime	J01DCO2	483.66
Piperacillin/tazobactam	J01CR05	433.67
Meropenem	J01DHO2	418.06
Ceftriaxone	J01DD04	305.55
Metronidazole	J01XD01	261.44
Levofloxacin	J01MA12	170.75
Azithromycin	J01FA10	101.67
Gentamicin	J01GB03	98.66
Cefotaxime	J01DDO1	46.29
Vancomycin	J01XA01	40.52
Augmentin	J01CR02	24.65
Erythromycin	J01FA01	22.70
Imipenem	J01DH51	19.61

DDD = defined daily dosage; ATC = anatomical therapeutic chemical.

Table 4. Comparison of antibiotic usage

Category	Duration, range (days)	Mean (SD), (days)
1st antibiotic (n=153)	1 - 21	6.92 (3.9)
2nd antibiotic (n=96)	1 - 39	7.5 (5.1)
3rd antibiotic (n=32)	1 - 14	5.6 (3.0)
4th antibiotic (n=8)	2 - 10	5.13 (2.4)

SD = standard deviation.

were used in 37 patients (24.7%), while 8 patients (5.2%) received the maximum of 4 antibiotics.

All patients admitted to the ICU received antibiotics, irrespective of their infective status. Since the antimicrobial choice was made by the clinicians (including the parent units as well as the intensivists) devoid of a standard protocol, it was difficult to quantitate the inappropriate use of antimicrobials. There were no correlations between the culture and

sensitivity reports and the usage of antimicrobials in individual patients, and there was no evidence of de-escalation of antimicrobials in any patient during the study period.

Discussion

Surveillance of microbes and their resistance patterns is invaluable in infection control and prevention in hospital medicine. Data regarding microbial spectrum and antimicrobial usage in different settings also help to compare these factors in developed and developing countries. The present study was able to achieve these objectives.

The demographics of the patients in the present study were similar to those in a study from the neighbouring island Barbados.^[12] There was a significant relationship between increased WBC and mortality in this study. WBC has been shown to be a clinical marker of inflammation and infection, and is considered an independent predictor of all-cause mortality in a previous report.^[13]

Increased length of ICU stay is generally associated with increased infection rates, contributing to higher mortality risk and increased cost of illness.^[14,15] This study did not, however, show a significant difference in this regard. Overall, the length of ICU stay of patients in the present study was comparable to that of previous reports originating from Barbados and China.^[12,16]

Blood was the most frequently sent specimen for bacteriological culture in the present study. This differs from the Barbados study, where tracheal aspirates were the most common specimens.^[12] Unlike in the Barbados research, in the present study not all patients were routinely sampled for microbiological cultures on admission, and many patients did not have such investigations during their whole ICU stay, unless signs of respiratory infection were evident, such as a change in the nature of tracheal secretions or radiological evidence suggestive of chest infection.

The majority of the tracheal aspirates yielded Gram-negative bacilli. *P. aeruginosa* was one of the most common organisms, as was found by a study from the USA that reported *Pseudomonas* and *Klebsiella* as the most common organisms.^[17] A report from Serbia also found Gram-negative organisms such as *Pseudomonas* and *Acinetobacter* to be the most common organisms in hospital-acquired pneumonias.^[18] Studies from ICUs in Egypt and India found *Klebsiella* to be the most common organisms associated with ventilator-associated pneumonia (VAP).^[19,20] The ICU where the present study was conducted does not formally adhere to any 'ventilator care bundle', and VAP rates might have been underestimated. However, endotracheal-tube colonisation by *Pseudomonas* is a well-established phenomenon; a recent study investigating the microbiome of endotracheal tubes showed that the presence of *Pseudomonas* in the endotracheal tube showed a strong correlation with the poor prognosis of ICU patients.^[21]

A small percentage of patients also grew MRSA from their tracheal aspirates. Although it has been previously reported, the prevalence of MRSA in hospital-acquired pneumonia is still low.^[22]

S. maltophilia was grown in two specimens. This opportunistic pathogen primarily infects immunocompromised patients, is often multidrug resistant and is considered to be an independent risk factor for mortality.^[23] In this study, both patients who had this infection died despite the organism's susceptibility to quinolones and aminoglycosides. The laboratory did not test the susceptibility of this organism for trimethoprim-sulfamethoxazole owing to lack of disks, and hence the susceptibility to this drug could not be ascertained.

Candida spp. and Gram-negative bacilli were the most prominently grown organism from the urine specimens, comparable with previous reports from different regions of the world.^[16,24]

S. epidermidis was grown from more than 50% of the blood specimens. This was the most common organism grown from CVC tips as well. It is often regarded as a commensal, unless its growth is associated with infective signs. The high rates may be due to contamination as a result of poor aseptic techniques when obtaining the samples.

Wound swabs from burns and surgical wounds cultured *P. aeruginosa* and MRSA as the most common organisms. In comparison, the most common isolates for wound swabs were *Enterobacteriaceae*, *P. aeruginosa* and *S. aureus* in Barbados.^[12]

In the present study, *P. aeruginosa* showed high sensitivity to quinolones and aminoglycosides. *Acinetobacter* commonly demonstrates multi-antimicrobial-resistance patterns. In the present study, it showed high sensitivity to quinolones, aminoglycosides and imipenem.

Enterobacteriaceae showed high susceptibility to aminoglycosides and penicillins. However, resistance rates were highest for cephalosporins. *Enterobacteriaceae* are well known to be resistant to third-generation cephalosporins.^[25]

The most common antimicrobial used overall in the ICU in this study was cefuroxime, followed by piperacillin/tazobactam and meropenem. Imipenem use was significantly lower than meropenem.

Cefuroxime is often used for surgical prophylaxis, and is continued on the general wards as well. This was shown in a previous study in the same hospital, which revealed a high frequency of prescriptions for cephalosporins on the adult and paediatric medical and surgical wards.^[26] In Barbados, the most commonly used antibiotic in their ICU was cefazolin, and this remained consistent during the 3-year period of the study.^[12] A study in Brazil also showed similar antimicrobial-usage patterns, with high cephalosporin prescription.^[27] Such high cephalosporin usage may simply be explained by the fact that there is greater familiarity with the drug, and represents choice based on physician preference rather than being evidence based.

The fact that sensitivity to piperacillin/tazobactam is generally higher than sensitivity to cephalosporins may point towards an inappropriate use of cephalosporins in the study hospital. This is not a problem unique to this hospital; it has also been demonstrated in a tertiary hospital in Port of Spain, the capital city of Trinidad, where there was inappropriate third-generation cephalosporin use in medical, surgical, gynaecological and orthopaedic wards.^[28]

In our situation, such inappropriate antimicrobial use might also be explained by the absence of an antimicrobial protocol. Also, there is a lack of culture-directed antimicrobial usage, which has implications for the poor de-escalation practices. This results in prolonged, indiscriminate use of broad-spectrum antimicrobials. In addition, this hospital does not have a clinical microbiologist or pharmacist assigned to the ICU to help to guide prescription practices.

The present study had some limitations, the major one being the retrospective design. Missing samples and documentation are commonly encountered in chart reviews, which may impact the findings. In addition, there were some pitfalls unique to the setting, in the guidelines for obtaining samples. For example, tracheal aspirates were the only form of specimens for respiratory infections. Given their low specificity to differentiate colonisation from infection in this sample, bronchoalveolar lavage (BAL) specimens might have been much more informative; however, the ICU did not have a protocol of collecting BAL specimens. This could possibly have led to some overtreatment. Shortage of testing disks for many drugs was also another limitation.

Nevertheless, the present study was able to report the spectrum of microbial growth in the ICU of a tertiary hospital in Trinidad and

Tobago. It also showed that the overall usage of antimicrobial agents was inappropriate in most instances. This clearly points to a need for improved regular surveillance, the institution of a multidisciplinary team to guide usage and also a need to establish an antimicrobial protocol and guidelines for this ICU.

Conclusion

Routine microbial surveillance, implementation of an antimicrobial protocol, developing guidelines to regulate the use of antimicrobials and input from infectious-disease specialists are necessary in every ICU setting to contain the development of multidrug-resistant organisms.

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