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Original article

Antimicrobial susceptibility among aerobic bacteria isolates in the Intensive Care Unit of a tertiary regional hospital in Trinidad & Tobago.

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ABSTRACT

Background: There are variations in the epidemiology, prevalent pathogens and antimicrobial susceptibility patterns of infections in the intensive care unit (ICU) from one health care facility to another, hospital to hospital, and country to country. This study was undertaken to determine and document the frequency of occurrence of microbial isolates and their antibiotic susceptibility pattern from clinical specimens received from the ICU of a tertiary regional hospital in Trinidad and Tobago.

Materials & methods: Microbial isolates from patients admitted to the ICU of the Eric Williams Medical Sciences Complex over a 4-year period were investigated. Automated systems and Standard microbiological methods including BACTEC 9240 (Becton-Dickinson Microbiology Systems), MicroScan Walk Away 96 SI (Dade Behring, USA), modified Kirby Bauer disc diffusion and Etest were used. Clinical specimens from 1,128 patients admitted to the ICU during the study period were processed, and 869 pathogens were recovered from 638 positive cultures.

Results: The most frequent pathogens were recovered from respiratory tract specimens, while the *Enterobacteriaceae* groups of organisms were the most prevalent isolates. Except for *Acinetobacter* species that exhibit a consistent multiple drug resistant patterns, all the pathogens showed variable susceptibility to the readily available antimicrobials in the country. A 4.2% incidence rate of ESBL producers was encountered among the *K. pneumoniae* and *E. coli* isolates from the unit. Methicillin-resistant *S. aureus* was noted to be on the decline in this unit, but we observed the emergence of genuine vancomycin resistant methicillin-resistant *S. aureus.*

Conclusions: Although *Enterobacteriaceae* and *Pseudomonas aeruginosa* were the most frequent isolates, there are still sufficient treatment options for patients infected with these organisms in the unit. Continuous surveillance and monitoring for multiple drug resistant pathogens in the unit should still be paramount especially with the ongoing establishment of the National Oncology Center and National Organ Transplant Units at the complex. There is an equal need for further studies on the determinants of drug resistance in this unit.

Key words: ICU, Trinidad & Tobago, *Enterobacteriaceae*, *Pseudomonas aeruginosa*, MRSA.

INTRODUCTION

Understanding the epidemiology of the most prevalent pathogens, sites of recovery, and the antimicrobial susceptibility pattern of the microbial isolates from clinical specimens from the intensive care unit (ICU) is an important factor in detecting major changes in the aetiology of infections and the emergence of multiple drug resistant organisms. Surveillance in the ICU is essential to infection control programs in that unit as it greatly assists in identifying outbreaks, frequent pathogens and their susceptibility patterns and it serves as a strong motivation to achieve effective infection control policies [1-3].

The epidemiology, prevalent pathogens and antimicrobial susceptibility patterns of infections in the ICU differ from one health care facility to another, hospital to hospital, and country to country [4]. Awareness of relevant pathogens is of value in (a) determining and selecting empirical antimicrobial therapy to treat presumed infection pending a microbiological confirmation of diagnosis; (b) decrease morbidity, mortality, overall cost and burden on the health care system; (c) and direct the development of guidelines for infection control measures [5-7]. Microbial agents isolated from an intensive care unit among other factors, affect the outcome of infection in patients admitted to the unit [8].

In 1998, Orrett reported the results of an 18-month

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study on pathogens and their susceptibility pattern from nosocomial ICU infections conducted at the Eric Williams Medical Sciences Complex (EWMSC) when it operated as a private hospital [9]. The present study was undertaken to determine and document the frequency of occurrence of microbial isolates and their antibiotic susceptibility pattern from clinical specimens received from the EWMSC intensive care unit now that the hospital operates as a tertiary health care facility serving a wider sector in the island. This data can be expected to guide empiric therapy decisions and to increase the confidence level of clinicians in their choice of antimicrobials.

MATERIALS AND METHODS

Study site

This cross sectional study was carried out on 1,472 clinical specimens received from the ICU of the EWMSC, Trinidad & Tobago from September 1, 2003 to August 31, 2007.

A 560-bed hospital offering services to patients from both public and private health institutions, the EWMSC is a referral tertiary center for the north central regional health facilities in the country. The complex is currently being expanded to accommodate facilities for the National Organ Transplant Unit (NOTU) as well as the National Oncology Centre (NOC). The ICU of the hospital has 10 beds that are available to serve all categories of patients coming from the different hospital departments. Of the 1,128 patients admitted to this facility during the study period, less than a quarter (23.3%, 263/1128) required mechanical ventilation.

Clinical specimens

Of 45,451 specimens received at the microbiology laboratory of the EWMSC during the study period, only 3.2% (1472/45,451) were from the 1,128 patients admitted to the ICU. More than half, or 54.1%, (796/1472) of these specimens came from male patients, 45.2% (665/1472) from female patients and the rest 0.7% (11/1472) from inanimate objects (such as air condition units vents, swabs from respiratory machines, wash hand sinks, beds and floors of the space in the ICU).

Blood stream specimens (376 samples) received from the ICU were incubated with BACTEC 9240 (Becton-Dickinson Microbiology Systems) for 5 days. Respiratory tract specimens (367), urinary tract specimens (363), skin and soft tissue specimens (253), CSF and stool specimens (113) were all processed following standard microbiological procedures [10]. Urinary catheter tip specimens were not processed, as this was a waste of meager resources and time. In addition, this is not recommended because a positive urinary catheter tip culture is not an acceptable laboratory test result to diagnose a urinary tract infection [11]. Duplicate specimens and isolates with the same antimicrobial resistance pattern recovered from the same patient were also excluded.

Antimicrobial susceptibility testing

Antimicrobial susceptibility tests were performed using the MicroScan Walk Away 96 SI (Dade Behring, USA) and modified Kirby Bauer disc diffusion method on Mueller-Hinton agar. Etest method was used to confirm the production of ESBL among the *K. pneumoniae* and *E. coli* isolates. Isolates of MRSA that the MicroScan system detected as resistant to vancomycin were further tested using the disc diffusion agar method. Minimum inhibitory concentrations were interpreted according to approved CLSI breakpoints [12]. Isolates with MIC breakpoints in the resistant and intermediate categories were regarded as having decreased susceptibility. Susceptibility tests were not carried out for coagulase-negative Staphylococci isolates.

Quality control was performed using reference strains of E. coli ATCC 25922, *K. pneumoniae* ATCC 700603 (ESBL positive), MRSA ATCC 43300, *S. aureus* ATCC 25923 and *P. aeruginosa* ATCC 27853 to confirm consistence of methods, materials and results. No analysis was done to determine whether the isolates encountered caused infection or only colonized these ICU patients. The data were analyzed using the Epi Info 3.2 software [13]. Since the data were descriptive, they were just reported as frequency of distributions.

RESULTS

Eight hundred and sixty nine pathogens were recovered from 43.3% (638/1472) of the specimens that had positive culture and more than half of these were Gram-negative organisms. The body site showing the highest frequency of isolation of pathogens was the respiratory tract (32.9%). This was followed by skin and soft tissue (32.1%), bloodstream (20.1%) and urinary tract (13.9%). The remaining (1%) was from cerebrospinal fluid, stools and genital tract specimens.

Table 1 shows the ranking of frequency of occurrence of the various genus and species groups of pathogens isolated from the clinical specimens. The most frequent isolates were *Enterobacteriaceae* (24.7%) and *Pseudomonas aeruginosa* (21.9%).

Antibiogram profiles of the most common isolates are shown in Table 2. More than 91% of the *P. aeruginosa* isolates were susceptible to all the aminoglycosides and fluoroquinolones agents tested; and more than 70% of the *P.*

aeruginosa isolates were susceptible to most of the anti-pseudomonas agents (piperacillin/tazobactam, ceftazidime, imipenem and meropenem) readily available on the island. *Acinetobacter* species susceptibility pattern revealed high rates of resistance to piperacillin/tazobactam (80%); ceftriaxone (92.5%), ceftazidime (87.5%), cefuroxime (89.5%), aztreonam (93.5%) and cefotaxime (100%). Resistance to fluoroquinolone was equally high, i.e. 70% for ciprofloxacin and 88% for levofloxacin. The isolates showed complete susceptibility to imipenem (100%) but only 71% to meropenem. Aminoglycosides were still an excellent choice for use in treating infections caused by the species as Amikacin and tobramycin had a susceptibility rate of 94% and 87% respectively.

Table 1: Distribution of 869 microbes recovered from 638 positive-culture clinical specimens from ICU patients at a tertiary hospital in Trinidad & Tobago, 2003-2007

Organism	Total (%)
Enterobacteriaceae[A]	216 (24.8)
Pseudomonas aeruginosa	190 (21.9)
Coagulase negative Staphylococci	137 (15.8)
Fungi species[B]	91 (10.4)
Staphylococcus aureus	78 (9.0)
Acinetobacter species	76 (8.7)
Pseudomonas species	29 (3.3)
Streptococcus species	18 (2.1)
Bacillus species	17 (2.0)
Stenotrophomonas maltophilia	8 (1.0)
Bulkhoderia cepacia	5 (0.6)
Moraxella catarrhalis	2 (0.2)
Micrococcus	1 (0.1)
Trichomonas vaginalis	1 (0.1)
Total	869

A = includes 86 isolates of Enterobacter species, 54 Klebsiella species, 30 E. coli, 16 Citrobacter species, 14 Serratia species, 11 Proteus species, 4 Providencia species and 1 Salmonella species. B = includes 51 isolates of *C. albicans*, 38 non-albicans candida and 2 Aspergillus species

For the *Enterobacteriaceae* species, all *Enterobacter* species isolated were fully resistant to ampicillin and amoxycillin-clavulanate signifying that these antimicrobial agents have no place or use in the treatment of infections caused by such organisms. More than 70% of the *Enterobacter* species were equally resistant to piperacillin, cefuroxime, ceftriaxone and ceftazidime. However over 80% of them were susceptible to cefepime, imipenem and ciprofloxacin, and over 70% were susceptible to the fluoroquinolone. All the *Enterobacter* species were completely susceptible to meropenem. All the ESBL producing *Enterobacteriaceae* isolates from this unit were 4.2%, comprising *E. coli* 2.1% and *K. pneumoniae* 8.2% respectively.

As depicted in Figure 1, methicillin resistant *S. aureus* isolates were still highly susceptible to several antimicrobials agents such as imipenem (83%), ciprofloxacin (76%) and linezolid (100%). Surprisingly, an 11% frequency of resistance was observed in Vancomycin among the MRSA

Table 2: Antimicrobial susceptibility profile among the most frequent Gram-negative bacterial isolates from the ICU of a tertiary hospital in Trinidad & Tobago, 2003-2007.

Antimicrobial	Percentage of isolates susceptible				
	P. aeruginosa	Enterobacter spp	Acinetobacter spp	Klebsiella spp	*E. coli*
Piperacillin	65.2	28.2	41.2	33.3	0
Pip/Tazo	76.7	48.6	20	75	100
Ceftazidime	73.0	22.7	12.5	0	26.2
Ceftriaxone	Na	20	7.5	72.3	100
Cefipime	60	87.5	Na	Na	Na
Cefuroxime	Na	10	10.5	65.6	76.5
Cefotaxime	Na	Na	0	Na	Na
Imipenem	74.2	82.6	100	100	66.7
Meropenem	71	100	71.1	100	80
Aztreonam	49.3	14.3	6.7	33.3	66.7
Gentamicin	92.5	54.5	43.2	73.3	84.2
Tobramycin	91.5	65	86.9	71.9	88.9
Amikacin	95.1	70.6	93.5	100	100
Ciprofloxacin	92.4	80	29.6	87.9	80
Norfloxacin	100	73	Na	80	100
Levofloxacin	91.5	77.8	12.5	81.8	100
Trim/Sulph	Na	74.1	19	76.9	90

Pip/Tazo = Piperacillin/Tazobactam; Trim/Sulph = Trimethoprim/Sulphamethazole; Na = not tested

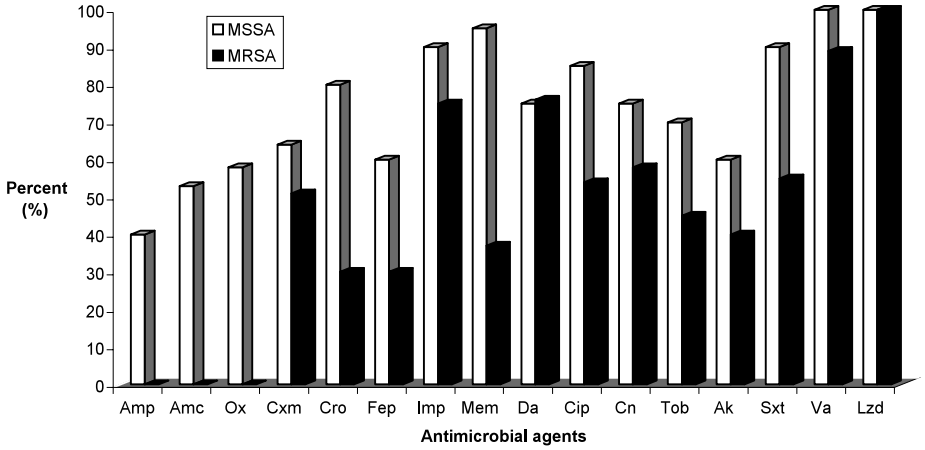

Figure 1: Antibiotic susceptibility pattern of *S. aureus* isolates from the Intensive Care Unit of a tertiary hospital in Trinidad & Tobago, 2003-2007

Amp − ampicillin, Amc − amoxicillin/clavulanate, Ox − oxacillin, Cxm − Cefuroxime, Cro − ceftriaxone, Fep − cefepime, Imp − imipenem, Mem − meropenem, Cip − ciprofloxacin, Da − clindamycin, Cn − gentamicin, Tob − tobramycin, Ak − amikacin, Sxt − trimethoprim/sulphamethazole, Va − vancomycin, Lzd − linezolid

isolates. The results also show that methicillin sensitive *S. aureus* (MSSA) isolates have over 75% susceptibility to several readily available antimicrobial agents in the country including carbapenems (imipenem, meropenem), cephalosporins (cefuroxime, cefepime), fluoroquinolone (ciprofloxacin), and aminoglycoside (gentamicin).

DISCUSSION

This study evaluated the frequency of occurrence and patterns of susceptibility to antimicrobial agents among pathogens recovered most frequently from clinical specimens from patients admitted to the ICU of the EWMSC. *Enterobacteriaceae* and *Pseudomonas aeruginosa* were the most frequent isolates. *Enterobacter* and *Klebsiella* species were the most frequent *Enterobacteriaceae* species, and the respiratory tract produced the highest number of isolates in the unit. These findings are similar to those reported elsewhere as well as the observations of Orrett at the same facility [14, 15, 1, 9]. Many factors could have caused the high frequency of isolation of these pathogens. These include the fact that the digestive tract is the reservoir for these organisms, that patients in ICU require prolonged assisted ventilation made possible through endotracheal intubations, and that these organisms spread easily through liquids and the respiratory devices. Other factors such as widespread environmental contamination have also been reported [16]. In view of this situation, the isolation of microbes from ICU patients requires timely, proper and accurate identification as to the aetiological pathogens implicated in the patient's condition. Clinical findings properly correlated with the institutional epidemiological and laboratory results will therefore be paramount.

The present study identified a high percentage of decreased susceptibility of ceftazidime antibiotic to the *Enterobacteriaceae.* This is consistent with findings coming from a study done by Hanberger et al [14]. The high prevalence of ceftazidime resistance among these pathogens may be due to extensive inappropriate use of cephalosporin in the country as reported by Pinto Pereira et al [17]. The prevalence of 4.2% ESBLs producers among isolates of *K. pneumoniae* and *E. coli* indicates the need for the judicious use of third generation cephalosporins and further surveillance of ESBL producers in the unit.

This study demonstrated that carbapenems are still highly effective for the members of the *Enterobacteriaceae*, which agrees with the report by Turner [18]. Carbapenems therefore are still relevant to use in our locality and continued surveillance is necessary to maintain them as choices in our ICU. Like findings reported elsewhere [14], there was a high rate of ceftazidime and imipenem use for *P. aeruginosa* in our study.

Isolates of *Acinetobacter* species were found to be multiresistant to most of the antimicrobial agents. This finding is similar to a report from a Spanish study where the species were equally multiresistant [19]. Though they are not the most virulent gram-negative pathogens, they may increasingly cause severe infections associated with a high rate of morbidity and mortality.

The prevalence of MRSA in the present study was 36%, which shows a huge decrease in comparison to a previous report at the same unit [9]. A good explanation for this is current infection control practices such as patient isolation, hand washing, use of gloves and appropriate gowns,

education and judicious use of antimicrobials. All these measures have been found to be necessary to prevent the emergence and spread of resistant pathogens [20-22]

The finding of MRSA isolates resistant to vancomycin in this study varies widely from what has been observed elsewhere [23] and even in previous reports from this same hospital and country [9, 23] where there has been no incidence of vancomycin resistance to MRSA isolates. In this unit and the country as a whole, the reasons for the incidence of vancomycin resistance to MRSA isolates are varied and many. Firstly, vancomycin has been available in the country for several years but has now suddenly become a wonder drug for treating all sorts of infections and is even given prophylactically in some hospital facilities. Secondly, there is great pressure on the use of vancomycin because of the frequent unavailability of the penicillinase resistant penicillin agents. Finally, linezolid, and other oxazolidinone and streptogramin agents are not yet in the national formulary and so often leave vancomycin as the only choice. A national policy on its use is now imminently needed in order to curtail any further increase in its resistance rate. In our previous report, it was concluded that vancomycin is still the drug of choice in treating multiple drug resistant MRSA infections [24]. With the findings of vancomycin resistance among the MRSA isolates in the present study, that conclusion can no longer hold.

CONCLUSION

In conclusion, the most frequent bacterial isolates were *Enterobacteriaceae* and *Pseudomonas aeruginosa*, and there are still sufficient treatment options for patients infected with these pathogens in the intensive care units of the EWMSC. The authors strongly recommend continuous surveillance and monitoring for the presence of multiple drug resistant organisms at the hospital especially now that the National Oncology Center and National Organ Transplant Units are being established at the complex. In addition, there is a need to carry out molecular studies to determine the mechanism of drug resistance in these isolates in the unit.

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