Microbial infection and antibiotic resistance patterns among Jordanian intensive care patients

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العدوى الجرثومية وأنماط مقاومة المضادات الحيوية بين مرضى وحدات العناية المركزة بالأردن

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خلاصة : لوحظ وقوع العدوى الجرثومية في 30% (155 من أصل 519) من جميع المرضى الذين أدخلوا تباعاً خلال سنة 1993 في وحدة العناية المركزة للكبار بمستشفى الجامعة الأردنية في عمان . ومن بين نوائب العدوى التي بلغ مجموعها 233 ، وجدت جراثيم سلبية غرام في 110 حالة (49%) ، وجراثيم إيجابية غرام في 69 حالة (31%) ، وأنواع مختلطة من الجراثيم في 25 حالة (11%) . كما وجدت أنواع المبيضات في19 حالة (9%) . وكانت أنواع الجراثيم الخمسة التي تم استفرادها أكثر من غيرها هي: العنقوديات الذهبية (40) والأسينوباكتر (28) والزوائف (22) والأمعائيات (20) والكلبسيلات (17) . ولوحظ أن المقاومة ضد المضادات الحيوية الشائعة تراوحت بين المتوسطة والشديدة بين المستفردات الإيجابية غرام والسلبية غرام على التوالي . ووجد أن الجراثيم السلبية للغرام كلها تقريبا كانت حساسة للدواءين إميبينيم وسيبروفلوكساسين .

ABSTRACT Microbial infections were observed in 30% (155/519) of all patients consecutively admitted in 1993 to the adult intensive care unit in the Jordan University Hospital in Amman. Gram-negative bacteria were involved in 110 (49%), Gram-positive bacteria in 69 (31%), mixed bacteria species in 25 (11%) and *Candida* spp. in 19 (9%) of all 223 infection episodes. Five species were isolated most frequently: *Staphylococcus aureus* (40), *Acinetobacter* spp. (28) *Pseudomonas* spp. (22), *Enterobacter* spp. (20) and *Klebsiella* spp. (17). Resistance to most commonly available antibiotics was moderate to very high among Gram-positive and Gram-negative isolates. Almost all Gram-negative bacteria were sensitive to imipenem and ciprofloxacin.

L'infection microbienne et les schémas de résistance aux antibiotiques chez les malades des services des soins intensifs en Jordanie

RESUME Des infections microbiennes ont été observées chez 30% (155/519) de l'ensemble des malades admis au service de soins intensifs pour adultes de l'Hôpital universitaire de Jordanie à Amman en 1993. Pour les 223 cas d'infection enregistrés en tout, il s'agissait dans 110 cas de bactéries à Gram négatif (49%), dans 69 cas de bactéries à Gram positif (31%), dans 25 cas d'espèces bactériennes associées (11%) et dans 19 cas de *Candida* spp (9%). Cinq espèces bactériennes ont été isolées plus fréquemment: *Staphylococcus aureus* (40), *Acinetobacter* spp (28), *Pseudomonas* spp (22), *Enterobacter* spp (20), et *Klebsiella* spp (17). La résistance à la plupart des antibiotiques couramment disponibles était de modérée à très forte parmi les isolats à Gram positif et négatif respectivement. Presque toutes les bactéries à Gram négatif étaient sensibles à l'imipénème et la ciprofloxacine.

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Introduction

Infection caused by multidrug-resistant bacteria constitutes a serious problem for intensive care patients throughout the world [*1–4*]. The mortality rate associated with multidrug-resistant Gram-negative enteric bacteria in these patients is high in some intensive care units (ICUs). It is likely that patterns of microbial infection and antibiotic resistance in ICU patients differ widely from one hospital or country to another and are often facilitated by the increasing use of invasive techniques, immunosuppressive drugs and inappropriate antibiotic therapy [*1,4–7*]. In addition, certain types of pathogens are becoming common in each local community and represent an important risk factor for the morbidity and mortality of ICU patients [*2,3,8*].

Patients and methods

The objective of this study was to investigate the incidence of microbial infection in association with antibiotic resistance among patients consecutively admitted to the adult ICU in the Jordan University Hospital in Amman over a one-year period. Patients in the ICU were considered to have an infection when clinical findings were confirmed by any culture-positive clinical specimen taken after at least a 24-hour stay in the ICU.

All clinical isolates were first identified by conventional methods in a routine microbiology laboratory [*9*]. A large representative number of Gram-negative isolates were subsequently identified at the species level with API 20E and API 20NE (Bio Merieux Systems, France).

Antibacterial susceptibility testing was first performed for all isolates by a disk diffusion method on Mueller–Hinton agar [*10*]. Antibiotic disks were obtained from Biolife (Italy). Multiple bacterial isolates from a single patient with the same resistance patterns were considered as one isolate for studying minimum inhibitory concentration (MIC) using Micro Scan, Type TN dried panel (Baxter Health Care Corporation, West Sacramento, California, USA). Minimum inhibitory concentrations were interpreted according to approved break points [*10*].

Differences between groups were considered statistically significant if P values were ≤ 0.05.

Results

During the one-year study, 519 consecutive patients were admitted to the ICU in the Jordan University Hospital. Of these, 155 (30%) showed evidence of infection as demonstrated by culture and clinical findings during their stay in the ICU.

The sites of infection and types of organisms recovered from the 155 patients are shown in Table 1. In all, 223 infection episodes were found in the clinically infected patients. Gram-negative bacteria were involved in 110 (49%; $P \leq 0.05$)of these episodes, Gram-positive bacteria in 69 (31%; $P \leq 0.05$), mixed bacteria species in 25 (11%) and *Candida* spp. in 19 (9%). The four leading sites of infection were skin and soft tissue (46%), respiratory tract (33%), urinary tract (14%) and blood (7%). The isolated pathogens, in descending order, were: *Staph. aureus* (40); *Acinetobacter* spp. (28); *Pseudomonas* spp. (22); *Enterobacter* spp.(20); coagulase-negative staphylococci (19); *Candida* spp. (19); *Klebsiella* spp. (17), *Escherichia coli* (15) and enterococcus (5).

The antibiograms of common isolates of Gram-negative bacteria using the mini-

Table 1 **Distribution of organisms isolated from 155 infected patients admitted to the intensive care unit, Jordan University Hospital**

Organism	Site of infection*				Total
	Blood	Respiratory tract	Urinary tract	Skin or soft tissue	
Gram-negative					
Acinetobacter spp.	1	14	4	9	28
Pseudomonas spp.	2	15	3	2	22
Enterobacter spp.	2	–	5	13	20
Klebsiella spp.	–	11	4	2	17
E. coli	1	2	6	6	15
Other	8	2	1	1	4
Total	8	43	23	36	110 (49%)
Gram-positive					
Staph. aureus	2	6	2	30	40
Coagulase-negative staphylococci	2	3	–	14	19
Enterococcus	–	–	1	4	5
Other	2	1	1	1	5
Subtotal	6	10	4	49	69 (31%)
Mixed bacteria	–	9	2	14	25 (11%)
Candida spp.	1	11	3	4	19 (9%)
All isolates	15 (7%)	73 (33%)	32 (14%)	103 (46%)	223 (100%)

** Six isolates from other body sites in the same patient(s) are considered as additional isolates in this table*

mum inhibitory concentration method are shown in Table 2. The majority of the isolates were highly resistant (66%–100%) to ampicillin and cephazolin, whereas resistance to other tested antibiotics varied (25%–90%) according to the species. However, most of these isolates were highly susceptible to imipenem and ciprofloxacin (0%–12% resistant) and to a less extent to amikacin (8%–29% resistant).

Coagulase-positive and -negative staphylococci were mostly moderately resistant to tested antibiotics except to penicillin drugs, where resistance was high (59%–83%) and to methicillin (35%–42%). However, all staphylococci isolates were susceptible to vancomycin (Table 3).

Discussion

In this study, the infection rate among ICU patients due to monoorganism or polyorganisms was 30%. Gram-negative bacteria were significantly more involved in infections (49%; $P \leq 0.05$) than Gram-positive bacteria, mixed bacteria and candida isolates. It is well documented that the higher rates of infection and mortality among ICU patients are mostly related to factors such as exposure to invasive procedures, underlying disease conditions, duration of stay in the ICU, infection sites and association with nosocomial multidrug-resistant pathogens [*1,3,6,8*]. Our study included both major infection sites and types of organ-

Table 2 **Antimicrobial susceptibility (MIC mg/l) of common multiple Gram-negative aerobic isolates from patients in the intensive care unit**

Organism (No. isolates)[a]	% of isolates resistant to the indicated antibiotic												
	Gm	To	Am	Crm	Caz	Cax	Cft	Imp	Azt	Aug	Pip	Cfz	Fox	Amk	Cp
Acinetobacter spp. (20)[b]	60	55	85	75	40	90	75	10	50	25	75	90	90	25	0
P. aeruginosa (17)	41	29	–	–	41	70	70	6	12	–	12	–	–	29	12
Erterobacter spp. (14)[c]	36	29	100	71	57	57	43	0	29	57	79	86	86	29	0
pneumoniae (13)	58	50	100	42	29	33	29	0	33	8	83	92	0	8	0
E.coli (12)	33	0	83	50	25	25	33	0	25	25	67	66	25	25	0

[a] *Only one isolate is identified to the species level if there are other similar isolates from the same patient*
[b] *Includes* A. baumanii *(18) and* A.Lwoffii *(2)*
[c] *Includes* E. cloacae *(7),* E. aerogenes *(5) and* E. agglomerans *(2)*
Gm=gentamicin; To=tobramycin; Am=ampicillin; Crm=cefuroxime; Caz=ceftazidime; Cax=ceftriaxone; Cft=cefotaxime; Imp=imipenem; Azt=aztreonan; Aug=Augmentin; Pip=piperacillin; Cfz=cefazolin; Fox=cefoxitin; Amk=amikacin; Cp=ciprofloxacin

isms and their susceptibility to commonly-used antibacterial agents in the developing country of Jordan, but it did not attempt to investigate the underlying disease conditions of patients or the role of nosocomial infection.

The common infection sites in the present study were skin and soft tissue, followed by respiratory tract, urinary tract and blood. Species of *Staphylococcus, Acinetobacter, Pseudomonas, Enterobacter, Klebsiella* and *Candida* were the most prevalent pathogens recovered from our ICU patients (Table 1).

A multicentre study conducted in 13 European countries in 1992 [*2*] indicated that respiratory tract samples (39%) were the most frequent source of bacterial isolates, followed by blood (21%) and urinary tract samples (17%). The predominant bacterial isolates reported in the European study were similar to our results and Gram-positive isolates were found to account for about 35% of all isolates. The European study also revealed that the most common Gram-negative isolates were *E. coli (17%), P. aeruginosa, (12%), K. pneumoniae (10%) and Enterobacter* spp. *(8%).* Most of the available data on infections among ICU patients were collected in industrialized countries at least 10 years ago [*10*]. These studies reported overall infection rates and mortality rates between 10% and 50% [*11,12*].

Numerous studies have shown that multidrug-resistant bacteria, in particular aerobic Gram-negative bacteria, easily colonize the gastrointestinal tract and respiratory tract of hospitalized patients [*6,11*]. In addition, it is well known that multidrug-resistant bacteria are becoming increasingly prevalent in the hospital environment as a result of the extensive use of antibiotics [*1–3,13*]. The results of this study revealed that a few types of multidrug-resistant Gram-negative bacteria (*A. baumanii, P.*

Table 3 **Antimicrobial susceptibility of *Staphylococci* species isolated from patients in the intensive care unit**

Organism (No. of isolates)	% of isolates resistant to indicated antibiotic							
	Am	C	Ce	Cl	E	Gm	M	V
S.*aureus* (36)	83	22	53	47	42	22	42	Nil
Coagulase-negative staphylococci (17)	59	35	41	41	35	29	35	Nil

Am=ampicillin; C=chloramphenicol; Ce=cephalothin; Cl=clindamycin; E=erythromycin;Gm=gentamicin; M=methicillin; V=vancomycin

aeruginosa and *K. pneumoniae*) were the major cause of infection in our ICU patients during 1993. Many of the Gram-negative isolates were more than 25% resistant to the β-lactam drugs introduced in the early 1990s (ceftriaxone, ceftazidime, cefotaxime), and also to the much older aminoglycosides (amikacin, gentamicin, tobramycin). However, excellent activity against all Gram-negative isolates was shown for imipenem and ciprofloxacin. Neither of these drugs has been extensively used in the treatment of our patients. Of the other tested antibacterial drugs, only Augmentin and cefoxitin demonstrated excellent to good activity *in vitro* against *K. pneumoniae*, whereas aztreonam and piperacillin proved to be highly effective *in vitro* against *P. aeruginosa*. Reports from European countries and the United States of America indicate that extensive use of the new β-lactam and fluoroquinolone drugs has contributed to the rapid emergence of multidrug-resistant Gram-negative bacteria, particularly *Klebsiella* spp., *Enterobacter* spp., *Pseudomonas* spp. and *Acinetobacter* spp. [*1,14–16*].

The present study demonstrated that staphylococci, enterococci and fungi did not cause serious infections such as septicaemia or meningitis among our ICU patients.

In conclusion, we suggest that the most important strategies for controlling the problem of multidrug-resistant organisms in any ICU should be directed towards continuously monitoring the presence of these organisms, and the avoidance of excessive or continued use of any single drug over a long period of time.

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