Antimicrobial-resistant bacteria in a general intensive care unit in Saudi Arabia

Nermin K. Saeed, MBChB, (D) ABMM, ***Abdulmageed M. Kambal,*** MBChB, FRCPath, ***Noura A. El-Khizzi,*** MSc, FRCPath.

ABSTRACT

الأهداف: تقييم مدى انتشار البكتيريا المقاومة لعدد من المضادات الحيوية والمسئولة عن حدوث العدوى لدى مرضى وحدة العناية المركزة في مستشفى القوات المسلحة بالرياض، فضلاً عن مراقبة كيفية مقاومتها لمضادات الميكروبات لمدة عام واحد.

الطريقة: أُجريت هذه الدراسة الاسترجاعية في مستشفى القوات المسلحة بالرياض، المملكة العربية السعودية وذلك خلال الفترة من يناير إلى ديسمبر 2009م. لقد قمنا بالرجوع إلى سجلات المرضى للتقصي عن مدى انتشار البكتيريا المقاومة للمضادات الحيوية والتي انقسمت إلى بكتيريا موجبة، وبكتيريا سالبة لصبغة غرام، وتمت دراسة مقاومتها لمضادات الميكروبات.

النتائج: لقد قمنا بجمع 1210 عينة ومن بينها كانت العينات التالية: 469 عينة من الجهاز التنفسي، و400 عينة من الدم، و235 عينة من الجروح، و56 عينة من البول، و35 مسحة من الأنف، و15 عينة من السائل الدماغي النخاعي. وقد أشارت النتائج إلى ارتفاع معدل انتشار البكتيريا المقاومة للمضادات الحيوية في العينات المعزولة من مرضى العناية المركزة بالرياض وذلك بصرف النظر عن المكان الذي عزلت منه هذه العينات، وعندما صنفت هذه البكتيريا وُجد أن البكتريا الراكدة الباومانية كانت تمثل 40.9% من العينات، بينما تمثل بكتيريا الكلبسيلة الرئوية نحو 19.4%، وتمثل البكتريا الزائفة الزنجارية حوالي 16.3%.

خاتمة: أشارت الدراسة إلى أن أكثر أنواع البكتريا شيوعاً بين العينات السريرية المعزولة من مرضى العناية المركزة كانت: البكتيريا الراكدة الباومانية، وبكتيريا الكلبسيلة الرئوية، والبكتيريا الزائفة الزنجارية، والبكتيريا الإشريكية القولونية، والمكوّرات العنقودية الذهبية (الحساسة والمقاومة للمثيسيلين) وكذلك المكورات العنقودية الذهبية الغير مفرزة للكوجيوليز. ولقد مثلت العينات المعزولة من الجهاز التنفسي نحو 39% من جميع العينات التي تم جمعها من وحدة العناية المركزة. وكانت أكثر أنواع هذه البكتريا انتشاراً هي البكتيريا الراكدة الباومانية وبكتيريا الكلبسيلة الرئوية.

Objectives: To assess the prevalence of multi-drug resistant (MDR) bacteria causing infections in patients at the intensive care units (ICUs) of Riyadh Military Hospital (RMH), as well as their antimicrobial resistance patterns for one year.

Methods: A retrospective, cohort investigation was performed. Laboratory records from January to December 2009 were studied for the prevalence of MDR Gram-negative and Gram-positive bacteria and their antimicrobial resistance in ICU patients from RMH, Riyadh, Kingdom of Saudi Arabia.

Results: A total of 1210 isolates were collected from various specimens such as: respiratory (469), blood (400), wound/tissue (235), urinary (56), nasal swabs (35), and cerebro-spinal fluid (15). Regardless of the specimen, there was a high rate of nosocomial MDR organisms isolated from patients enrolled in the General ICU (GICU) in Riyadh. *Acinetobacter baumannii (A. baumannii*) comprised 40.9%, *Klebsiella pneumonia (K. pneumonia*) - 19.4%, while *Pseudomonas aeruginosa* (*P. aeruginosa)* formed 16.3% of these isolates.

Conclusion: The *P. aeruginosa, A. baumannii*, *K. pneumoniae, Escherichia coli*, *Staphylococcus aureus (*methycillin sensitive and methycillin resistant), and *Staphylococccus* coagulase negative are the most common isolates recovered from clinical specimens in the GICU of RMH. Respiratory tract specimens represented nearly 39% of all the specimens collected in the ICU. The most common MDR organisms isolated in this unit were *A. baumannii,* and *K. pneumoniae*.

Saudi Med J 2010; Vol. 31 (12): 1341-1349

From the Microbiology Department (Saeed, Kambal), King Khalid University Hospital, and Microbiology Department (El-Khizzi), Riyadh Military Hospital, Riyadh, Kingdom of Saudi Arabia.

Received 5th October 2010. Accepted 8th November 2010.

Address correspondence and reprint request to: Dr. Nermin K. Saeed, Microbiology Department, King Khalid University Hospital, Riyadh, Kingdom of Saudi Arabia. Tel. +966 531677966. Fax. +966 (1) 4783033. E-mail: nkamalh@hotmail.com

Antibiotic bacterial resistance is becoming a worldwide increasing difficult problem in the intensive care units (ICUs).[1] Residents at long-term care facilities are one of the main reservoirs of antimicrobial-resistant bacteria.[2] There is a strong association between antimicrobial overuse and the emergence of antibiotic bacterial resistance with the highest prevalence in ICUs.[3,4] Previous epidemiological studies have focused primarily on 2 common Gram-positive (GP) antimicrobial-resistant organisms; methicillin-resistant *Staphylococcus aureus* (*S. aureus* [*MRSA*]) and vancomycin-resistant *Enterococci* (VRE).[5,6] Recent data from the United States showed that multidrug resistance (MDR) among Gram-negative (GN) bacteria is becoming even a greater problem in hospitals and other health care facilities, with nearly half of long-term care facility residents harboring MDR-GN bacteria.[7] The MRSA, VRE, *Clostridium difficile*, *Acinetobacter baumannii* (*A. baumannii*), *Stenotrophomonas maltophilia (S. maltophilia)*, *Serratia marcescens (S. marcescens)*, *Pseudomonas aeruginosa* (*P. aeruginosa*), *Klebsiella pneumoniae* (*K. pneumoniae*), and many others create huge problems in hospital practice with high rates of morbidity and mortality.[8] The emergence of MDR bacteria is an increasing problematic cause of hospital-acquired infections in ICUs, not only due to increased morbidity and mortality, but also due to the increased treatment costs as a result of frequent empirical antimicrobial therapy failure and lengthy hospital stay.[8-11] The increased mortality of MDR-GN infection may be due to the toxins secreted into the bloodstream that cause inflammation and destroy healthy tissues, which may be fatal if not properly treated.[12] Key factors in the management and prevention of MDR bacteria include restriction of antibiotic use, highlightening infection control standards of hand and environmental hygiene, surveillance, active patient and resource management, and education.[13] The purpose of this study was to assess the prevalence of MDR bacteria-causing infections in patients in ICUs, as well as their antimicrobial resistance patterns for a period of one year in one of the main general and tertiary care hospitals in Riyadh, Kingdom of Saudi Arabia (KSA).

Methods. A retrospective, cohort study was performed using laboratory records from a General ICU (GICU) of a tertiary care hospital in Riyadh, KSA from January to December 2009 to study the microbial pattern and types of GP and GN MDR bacteria isolated from ICU patients. Riyadh Military Hospital (RMH) is a 1200 beds, general tertiary care hospital, located in Riyadh, KSA. The studied unit is a 20-bed GICU. This is a closed unit with a multi-disciplinary care team that includes 6 full-time critical care consultants, 6 senior registrars, 15 registrars, 10 rotating internal medicine residents, 4 full-time respiratory therapists, and one ICU trained nurse for every patient at a time. The data were abstracted from the Laboratory Information System (CERNER, Classic 360, Kansas City, Missouri, USA). We included in the study all patients admitted to GICU, and excluded specimens with fungal or tuberculous isolates and duplicated samples with the same resistance patterns. The study was approved by the research and ethical committee of RMH.

Data pertaining to all microbial isolates and their antibiotic susceptibility data were retrospectively collected and entered into the Microsoft Excel Data-base. The data were analyzed separately for the predominant GN isolates, (*Escherichia coli [E. coli]*, *K. pneumoniae*, *P. aeroginosa*, *Acinetobacter spp*, and other non-fermenting GN bacteria) and GP isolates. The analysis was performed using TexaSoft, WINKS SDA Software 2007 (Sixth Edition, Cedar Hill, Texas, USA).

Bacteriologic testing methods. Identification of all causative microorganisms was performed by standard microbiologic methods (API 20 E and API 20 NE, BioMérieux, Marcy-l'Etoile, France).[14] The antimicrobial susceptibility testing was performed on all isolates received from GICU patients that were included in the study. The hospital Microbiology Laboratory performed susceptibility testing with an automated system (MicroScan, Walkaway 96 Microbiology Dade System, Siemens, New Jersey, USA). The breakpoint minimum inhibitory concentration (MIC) was determined for 15 antimicrobial agents: amikacin, ampicillin, amoxicillin-alavulanic acid, aztreonam, ceftazidime, ceftriaxone, cefuroxime, cefepime, imipenem, meropenem, piperacillin/tazobactam, ciprofloxacin, gentamicin, tigecycline, and trimethoprim-sulfamethoxazole. Clinical Laboratory Standards (CLSI) interpretive criteria were used for the interpretation of susceptibility results and breakpoints.[15] Susceptibility testing was performed using the disk-diffusion method for antibiotics, which were not on the Microscan panels (colistin, tigecycline, and cefoxitin). Presence of extended spectrum beta-lactamases (ESBL) was suggested by resistance to a third generation cephalosporins (cefotaxime, cefotriaxone or ceftazidime) in Microscan. Resistance to carbapenems for *P. aeruginosa* was checked by E-test for the involvement of metalo-β-lactamases. The disk diffusion method (10 μg of colistin sulfate disk) was used to test colistin susceptibility (Oxoid Ltd., Basingstoke, Hampshire, England).[1] The E-test technique using the same cutoff points was used to verify the results and to determine the resistant isolates (susceptible: 2 mg/l or less, resistant: 4 mg/l or more).[1] Molecular biologic studies were not performed to identify the similarity or dissimilarities of the microbial species of the bacterial isolates. Isolates

phenotypically similar from different specimens of the same patient were considered as one sample.

Definition of resistance. According to the *Falagas ME, Karageorgopoulos DE* system of MDR classification, MDR stains are those which showed resistance to 3 or more classes of antimicrobial agents.[16] Extensive drug resistant strains are those which showed resistance to all, but 1 or 2 classes of antimicrobial agents, while pan-drug resistant strains are those which showed resistance to all classes. For the purpose of this study and to avoid confusion, we defined MDR strains as those that exhibit resistance to 3 or more classes of antibiotics. The bacterial strains were defined to be penta-resistant if they showed resistance to 5 classes of antibiotics, while hepta-resistant if they showed resistance to 7 or more classes of antibiotics. Clinically Important Resistance (CIR) were recognized when such strains showed resistance to extended spectrum cephalosporins and fluoroquinolones.[16] We defined a strain of microorganism as pan-resistant if it did not exhibit susceptibility or reduced susceptibility to any of the antimicrobial agents tested.[1] When *A. baumannii, P. aeruginosa*, and *K. pneumoniae* strains showed resistance to 5 or more out of 7 anti-pseudomonal antimicrobial classes, they were classified as MDR.[1] The MDR strains of *Mycobacterium tuberculosis* were not addressed in this study.

Results. ***Patient demographics and specimen types.*** The total number of admissions to the GICU during this study was 1269 with a mean length of stay of 9.5 ± 17 days, and a mortality rate of 15%. The specimens were collected from 781 patients. Males were 486 (62.2%) while females were 295 (37.8%), with a male: female ratio of 1.6:1. There were 1210 isolates after exclusion of repeated samples with a sensitivity pattern collected from 469 respiratory specimens, 400 blood specimens, 235 wound/tissue specimens, 56 urinary specimens, 35 nasal swabs, and 15 cerebrospinal fluid (CSF) specimens. There were 796 GN bacilli isolates and 350 GP cocci isolates including duplicated isolates. The most common organisms isolated are shown in **Figure 1**. The most common GP cocci isolated was *S. aureus* (137/350), followed by *Staphylococcus* coagulase negative (STACN) (135/350). The most common GN bacilli isolated were: *P. aeruginosa*, *A. baumannii*, *K. pneumoniae*, *E. coli*, *Enterobacter cloacae*, *Serratia marcescens*, and *Stenotrophonomas maltophilia*, together made up to 62.1% of all bacterial isolates in the ICU. **Table 1** shows the most common isolates according to specimen sites, such as respiratory (38.8%), blood (33%), wound/tissue (19.4%), CSF (1.2%), and the urinary tract (4.6%??). The most common isolate from respiratory specimens was *P. aeruginosa* (32.6%), while the most common isolates from blood culture specimens was STACN (30.7%). The *S. aureus* was the most common isolate from wound and tissue specimens (20.9%), while *P. aeruginosa* was the most commonly isolated organisms from the urinary tract specimens (36.3%). The *P. aeruginosa* and *A. baumannii* form 66.7% of the CSF isolates, while *S. aureus* was the only isolated pathogen from the nasal specimens. **Table 2** shows the most common organisms isolated from the ICUs (710 sample included) after exclusion of repeated isolates for the same patient (500 samples excluded). The most common GN isolates were *A. baumannii* (28%), *P. aeruginosa* (26%), and *K. pneumoniae* (20%). In GP isolates, STACN was the most common isolate (45.3%) followed by MRSA (18%), and *E. faecium* (11.9%). **Table 3** shows the frequency and percentage of antibiotics resistance in GN bacilli. The

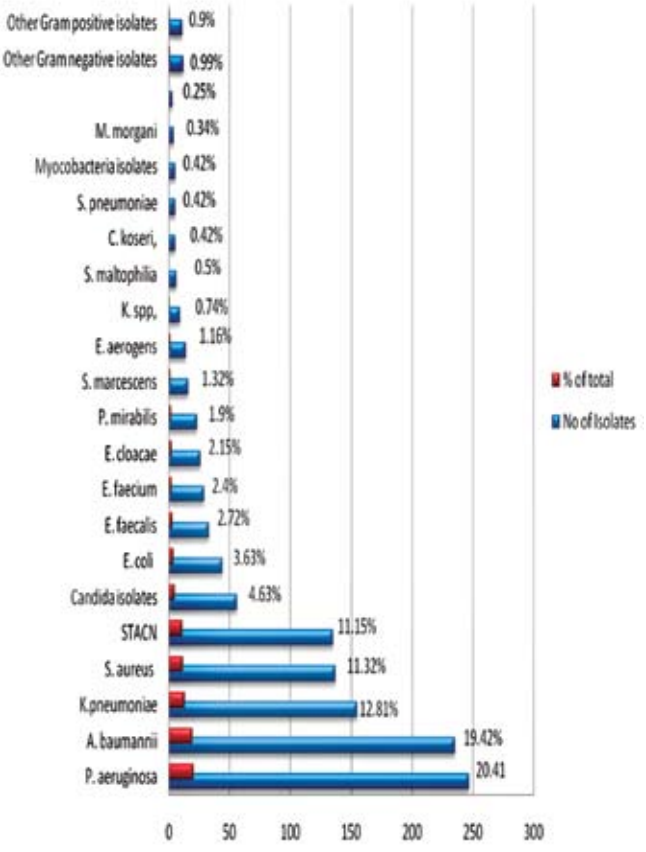

Figure 1 - Most commonly isolated organisms. *P. aeruginosa - Pseudomonas aeruginosa, A. baumannii - Acinetobacter baumannii; K. pneumoniae - Klebsiella pneumoniae; S. aureus - Staphylococcus aureus, STACN - Coagulase Negative Staph, E. coli - Escherichia coli, E. faecalis - Enterococcus faecalis; E. faecium - Enterococcus faecium, E. cloacae - Enterobacter cloacae; P. mirabilis - Proteus mirabilis, S. marcescens - Serratia marcescens; E. aerogenes - Enterobacter aerogenes; K. Spp - Klebseilla species, S. maltophilia - Stenotrophomonas maltophilia, C. Koseri - Citrobacter koseri, S. pneumoniae - Streptococcus pneumoniae, M. morganii - Morganella morganii.*

Table 1 - The most common organisms isolated from the intensive care unit by specimen site (N=1210).

Specimen site	n	(%)	Ranking	Organism	n	(%)
Respiratory	469	(38.8)				
			1	*P. aeruginosa*	153	(32.6)
			2	*A. baumannii*	142	(30.3)
			3	*K. pneumoniae*	50	(10.7)
			4	*S. aureus*	28	(6.0)
			5	*Candida*	23	(5.0)
			6	*E. coli*	11	(2.3)
			7	*S. marcescens*	9	(1.9)
			8	*STACN*	8	(1.7)
			9	*E. faecalis*	6	(1.3)
			10	*S. pneumoniae*	5	(1.1)
			11	*P. mirabilis*	3	(0.6)
			12	Other	31	(6.6)
Blood	400	(33.0)				
			1	*STACN*	123	(30.7)
			2	*K. pneumoniae*	63	(15.7)
			3	*A. baumannii*	40	(10.0)
			4	*P. aeruginosa*	38	(9.5)
			5	*S. aureus*	24	(6.0)
			6	*E. faecalis*	19	(4.75)
			7	*Candida*	19	(4.75)
			8	*E. coli*	15	(3.75)
			9	*E. faecium*	15	(3.75)
			10	*E. cloacae*	12	(3.0)
			11	*E. aerogenes*	7	(1.75)
			12	*P. mirabilis*	5	(1.25)
			13	*S. viridans*	3	(0.75)
			14	*S. marcescens*	3	(0.75)
			15	Others	14	(3.5)
Wound & tissue	235	(19.4)				
			1	*S. aureus*	49	(20.9)
			2	*A. baumannii*	48	(20.4)
			3	*K. pneumoniae*	31	(13.2)
			4	*P. aeruginosa*	29	(12.3)
			5	*Candida*	14	(6.0)
			6	*E. coli*	9	(3.8)
			7	*E. faecalis*	8	(3.4)
			8	*E. cloacae*	8	(3.4)
			9	*E. faecium*	7	(3.0)
			10	*P. mirabilis*	7	(3.0)
			11	*STACN*	3	(1.3)
			12	*S. milleri*	3	(1.3)
			13	Others	19	(8.1)
Urine	56	(4.6)				
			1	*P. aeruginosa*	20	(36.3)
			2	*K. pneumoniae*	11	(20.0)
			3	*E. coli*	8	(14.5)
			4	*E. faecium*	7	(12.7)
			5	*P. mirabilis*	4	(7.3)
			6	*A. baumannii*	2	(3.6)
			7	Other	4	(7.3)
CSF	15	(1.2)				
			1	*P. aeruginosa*	7	(46.7)
			2	*A. baumannii*	3	(20.0)
			3	Other	5	(33.3)
Nose	35	(2.9)		*S. aureus*	35	(100)

P. aeruginosa - Pseudomonas aeruginosa, A. baumannii - Acinetobacter baumannii, K. pneumoniae - Klebseilla pneumoniae, S. aureus - Staphylococcus aureus, E. coli - Escherichia coli, S. marcescens - Serratia marcescens, STACN - Staphylococcus coagulase negative, *E. faecalis - Enterococcus faecalis, S. pneumoniae - Streptococcus pneumoniae, P. mirabilis - Proteus mirabilis, E. faecium - Enterococcus faecium, E. cloacae - Enterobacter cloacae, E. aerogenes - Enterobacter aerogenes, S. viridians - Streptococcus viridians, S. milleri - Streptococcus milleri, CSF - cerebrospinal fluid*

highest resistance rates for *A. baumannii* were: for ampicillin, cefuroxime, and chloramphenicol (100%); followed by piperacillin/tazobactam (93.2%) and ciprofloxacin (92%), while the highest resistance rate for *P. aeruginosa* was for ceftazidime (43.9%) followed by imipenem (35.8%), and meropenem (33.6%). For *Enterobacter spp.*, the highest resistance rate was for Aug (amoxicillin/clavulanate) (94%), tigecycline (50%), aztreonam (43.7%) and piperacillin/tazobactam (43.7%). For *K. pneumoniae*, the highest resistance rate was for ceftriaxone (59.4%), aztreonam (58.3%), and ceftazidime (58.3%). Most GN isolates were sensitive to colistin. The highest resistance rate to colistin was observed in *Proteus mirabilis* (88%), *Morganella morganii* (66%) and *S. maltophilia* (17%). The highest resistance rate to tigecycline was observed in *A. Baumannii* (43%) and *E. cloacae* (50%). **Table** 4 shows the frequency and percentage of antibiotics resistance in Gram-positive isolates resistant to the antibiotics tested. No MSSA showed any resistance to chloramphenicol, fucidic acid, linezolid, mupirocin, netlimycin, rifampicin, teicoplanin and vancomycin, while the highest resistance rate was

Table 2 - The most common organisms isolated from the intensive care unit after exclusion of repeated samples from the same patients.

Rank	Organism	n	(%)
Gram-negative bacilli			
1	*A. baumannii*	133	(28.0)
2	*P. aeuroginosa*	123	(26.0)
3	*K. pneumoniae*	96	(20.0)
4	*E. coli*	39	(8.2)
5	*E. cloacae*	16	(3.3)
6	*P. mirabilis*	16	(3.3)
7	*S. marcescens*	9	(1.9)
8	*E. aerogenes*	8	(1.7)
9	*K. spp*	8	(1.7)
10	*S. maltophilia*	6	(1.3)
11	*Citrobacter*	5	(1.1)
12	*M. morgani*	3	(0.6)
13	Others	12	(2.5)
Total		**474**	**(100)**
Gram-positive cocci			
1	STACN	107	(45.3)
2	MRSA	43	(18.2)
3	*E. faecium*	28	(11.9)
4	*MSSA*	25	(10.6)
5	*E. faecalis*	22	(9.3)
6	Others	11	(4.7)
Total		**236**	**(100)**

A. baumannii - Acinetobacter baumannii, P. aeruginosa - Pseudomonas aeruginosa, K. pneumoniae - Klebseilla pneumoniae, E. coli - Escherichia coli, E. cloacae - Enterobacter cloacae, P. mirabilis - Proteus mirabilis, S. marcescens - Serratia marcescens, E. aerogenes - Enterobacter aerogenes, K. spp - Klebseilla species, S. maltophilia - Stenotrophonomas maltophilia, M. morgani - Morgamella morgani, STACN - *Staphylococcus* coagulase negative, MRSA - methicillin resistant *Staphylococcus aureus, E. faecium - Enterococcus faecium, E. faecalis - Enterococcus faecalis,* MSSA - methicillin sensitive *Staphylococcus aureus*

Table 3 - Number of resistant Gram-negative bacilli isolates compared with the total tested.

Organisms	*Acinetobacter baumannii*	*Pseudomonas aeuroginosa*	*Enterobacter. cloacae*	*E. Aerogenes*	*Klebseilla pneumoniae*	*Klebseilla species*	*Escherichia coli*	*Serratia marcescens*	*Proteus mirabilis*	*Citrobacter*	*Morganella morganii*	*S. maltophilia*
AK	115/133 (86)	19/123 (15)	1/16 (6)	0/8 (0)	8/96 (8)	0/8 (0)	4/39 (10)	0/9 (0)	4/16 (26)	0/5 (0)	0/3 (0)	6/6 (100)
Amp	133/133 (100)		16/16 (100)	7/8 (88)	96/96 (100)	8/8 (100)	36/39 (92)	9/9 (100)	1/16 (62)	5/5 (100)	3/3 (100)	6/6 (100)
AMP/SUL	81/129 (63)		10/16 (63)	4/7 (57)	68/91 (75)	5/8 (63)	25/37 (68)	9/9 (100)	10/16 (63)	5/5 (100)	1/3 (33)	6/6 (100)
Aug	128/133 (96)		15/16 (94)	7/8 (88)	52/96 (54)	3/8 (38)	15/39 (38)	9/9 (100)	6/16 (38)	3/5 (60)	3/3 (100)	6/6 (100)
Azt	113/133 (83)	22/123 (18)	7/16 (44)	3/8 (38)	56/96 (58)	4/8 (50)	19/38 (50)	3/9 (33)	7/16 (43)	2/5 (40)	1/3 (33)	6/6 (100)
Fep	113/131 (86)	33/121 (27)	6/16 (38)	1/7 (14)	53/94 (56)	2/8 (25)	21/39 (54)	3/9 (33)	6/16 (38)	0/5 (0)	1/3 (33)	6/6 (100)
Caz	117/133 (88)	54/123 (44)	9/16 (56)	3/8 (38)	56/96 (58)	2/8 (25)	19/39 (49)	4/9 (44)	8/16 (50)	2/5 (40)	1/3 (33)	3/6 (50)
CRO	120/132 (91)	80/122 (66)	10/16 (63)	3/8 (38)	57/96 (59)	4/8 (50)	19/39 (49)	4/9 (44)	8/16 (50)	3/5 (60)	1/3 (33)	6/6 (100)
CXM	133/133 (100)		12/16 (75)	5/8 (63)	64/96 (66)	5/8 (63)	22/39 (56)	9/9 (100)	8/16 (50)	5/5 (100)	2/3 (66)	6/6 (100)
CHL	131/131 (100)		4/15 (27)	1/8 (13)	20/95 (21)	2/8 (25)	7/39 (18)	4/9 (44)	8/16 (50)	1/5 (20)	1/3 (33)	3/6 (50)
CIP	122/133 (92)	27/123 (22)	6/16 (38)	0/8 (0)	40/96 (42)	3/8 (38)	20/39 (51)	2/9 (22)	9/16 (56)	1/5 (20)	1/3 (33)	4/6 (66)
COL	0/133 (0)	1/123 (8)	0/16 (0)	0/8 (0)	3/95 (3)	0/8 (0)	0/39 (0)	0/9 (0)	14/16 (88)	0/5 (0)	2/3 (66)	1/6 (17)
CN	105/132 (80)	28/123 (23)	3/16 (19)	1/8 (13)	53/96 (55)	2/8 (25)	15/39 (38)	2/9 (22)	12/16 (75)	2/5 (40)	1/2 (50)	6/6 (100)
IMP	82/92 (89)	44/123 (36)	0/16 (0)	1/8 (13)	3/96 (3)	1/8 (13)	0/39 (0)	0/9 (0)	1/16 (62)	0/5 (0)	1/3 (33)	6/6 (100)
MEM	120/132 (91)	41/122 (34)	0/16 (0)	1/8 (13)	3/95 (3)	1/8 (13)	0/39 (0)	0/9 (0)	0/16 (0)	0/5 (0)	0/2 (0)	6/6 (100)
NET	62/131 (47)	21/121 (17)	4/16 (25)	0/8 (0)	32/96 (33)	8/8 (13)	12/38 (51)	1/9 (11)	9/16 (56)	2/5 (40)	0/2 (0)	5/6 (83)
Pip-taz	124/133 (93)	33/123 (27)	7/16 (44)	3/8 (38)	46/96 (48)	4/8 (50)	10/39 (26)	3/9 (33)	1/16 (62)	1/5 (20)	0/2 (0)	6/6 (100)
SXT	75/133 (56)		5/16 (31)	0/8 (0)	53/96 (55)	3/8 (38)	26/39 (66)	3/9 (33)	14/16 (88)	1/5 (20)	1/3 (33)	0/6 (0)
Tig	42/98 (43)		2/4 (50)		1/22 (5)		0/4 (0)			1/1 (100)		
ESBL					23/25 (92)		5/5 (100)					

E. Aerogenes - Enterobacter aerogenes, S. Maltophilia - Stenotropohomonas Maltophilia, Ak - amikacin, Amp - ampicillin, AMP/SUL - ampicillin/sulbactam, AUG - augmentin, AZT - aztreonam, FEP - cefepime, CAZ - ceftazidime, CRO - ceftriaxone, CXM - cefuroxime, CHL - chloramphenicol, CIP - ciprofloxacin, COL - colistin, CN - gentamicin, IMP - imipenem, MEM - meropenem, NET - netilmicin, PIP-TAZO - piperacillin- tazobactam, SXT - co-trimoxazole, Tig -tigecycline, ESBL - extended spectrum beta lactamase ESBL - Extended Spectrum Beta Lactamase

Table 4 - Number of resistant Gram-Positive cocci isolates compared with total tested.

Antibiotic	Cocci n (%)			
	MSSA	MRSA	STACN	ENTFAEC	ENTFAE
Aug (amoxicillin/clavulanate)	1/25 (4.0)	43/43 (100)	95/107 (88.9)		
Ampicillin				20/22 (90.9)	3/28 (10.7)
Bacitracin	1/20 (5.0)	0/43 (0)			
Cefoxitin	1/25 (4.0)	43/43 (100)	95/107 (88.9)		
Chloramphenicol	0/25 (0)	3/41 (7.3)	11/107 (10.3)	8/22 (36.4)	12/28 (42.9)
Ciprofloxacin	1/25 (4.0)	28/41 (68.3)	60/107 (56.1)	21/21 (100)	24/28 (85.7)
Clindamycin	1/24 (4.1)	23/41 (56.1)	56/94 (59.6)		
Erythromycin	5/25 (20.0)	35/41 (85.3)	90/107 (84.1)		
Fucidin	0/5 (0)	5/5 (100)	80/90 (88.9)		
Gentamicin	1/24 (4.1)	20/41 (48.7)	70/107 (65.4)		
Linezolid	0/25 (0)	0/43 (0)	0/106 (0)	0/21 (0)	0/28 (0)
Methicillin	1/25 (4.0)	43/43 (100)	95/107 (88.9)		
Mupirocin	0/21 (0)	0/43 (0)			
Mupirocin200	0/20 (0)	0/41 (0)			
Netilmicin	0/7 (0)	5/6 (83.3)	6/96 (6.2)		
Oxacillin	1/24 (4.1)	43/43 (100)	94/107 (87.9)		
Rifampicin	0/24 (0)	7/41 (17.1)	28/107 (26.2)	20/22 (91.0)	0/28 (0)
Co-trimoxazole	1/24 (4.1)	19/43 (46.3)	9/10 (64.5)		
Teicoplanin	0/25 (0)	0/43 (0)	0/107 (0)	3/21 (14.0)	0/28 (0)
Tetracycline	2/23 (8.6)	17/40 (42.5)	15/87 (17.2)	14/22 (64.0)	24/28 (86.0)
Tigecycline				0/2 (0)	
Vancomycin	0/25 (0)	0/43 (0)	0/107 (0)	9/22 (40.9)	2/28 (7.1)

MSSA - methicillin sensitive *Staphyloccus aureus*, MRSA - methicillin resistant *Staphyloccus aureus,* STACN - Staphylococcus coagulase negative, ENTFAEC - *Enterococcus faecium*, ENTFAE - *Enterococcus faecalis,*
Please note: that not all isolates were tested with all antibiotics according to Microscan Data base. Colistin and Tigecycline were tested in cases of multidrug resistance isolates. Cefoxitin was used to check for methicillin resistant isolates.

Table 5 - Multi-drug resistant (MDR) among Gram-negative (GN) bacteria.

Ranking	Organism	Total MDR n (%)	Penta-resistant n (%)	Hepta-resistant n (%)
1	*Acinetobacter baumannii*	129 (40.4)	7 (2.2)	4 (1.2)
2	*Klebseilla pneumoniae*	62 (19.4)	29 (9.1)	19 (6.0)
3	*Pseudomonas aeruginosa*	52 (16.3)	12 (3.8)	9 (2.8)
4	*Escherichia coli*	27 (8.5)	13 (4.1)	1 (0.3)
5	*Proteus mirabilis*	12 (3.8)	4 (1.2)	6 (1.9)
6	*Enterobacter cloacae*	8 (2.5)	2 (0.6)	3 (0.9)
7	*Serratia. marcescens*	7 (2.2)	4 (1.2)	2 (0.6)
8	*Stenotrophonomas maltophilia*	6 (1.9)	0	6 (1.9)
9	*Enterobacter aerogenes*	5 (1.6)	1 (0.3)	1 (0.3)
10	*Other K. spp*	5 (1.6)	2 (0.6)	1 (0.3)
11	*Citrobacter koseri*	2 (0.6)	0	1 (0.3)
12	*Morgamella morganii*	2 (0.6)	0	1 (0.3)
13	Other GN isolates	2 (0.6)	0	0
Total		**319 (100)**	**74 (23.2)**	**54 (16.9)**

K. spp - Klebseilla species, Penta-resistant bacteria - strains that exhibit resistance to 5 classes of antibiotics, hepta-resistant bacteria - strains that exhibit resistance to 7 or more classes of antibiotics

revealed to be for erythromycin (20%) and tetracycline (9%). For MRSA, there was no resistance to bacitracin, linezolid, muprocin, teicoplanin and vancomycin. The highest resistance rate in MRSA was for oxacillin (100%), amoxicillin/clavulanate (100%) and methicillin (100%). The highest resistance rate for STACN was for fucidic acid (89%), amoxicillin/clavulanate (88.9%), oxacillin (87.9%), and erythromycin (84.1%). For *Enterococcus species*, 7.1% of *E. fecalis* were vancomycin-resistant, while 40.1% of *Enterococcus faecium* (*E. faecium*) were vancomycin resistant. However, both *E. fecalis* and *E. faecium* showed no resistance to linezolid. Tigecycline was tested only in 2 cases of *E. fecalis* and both cases were resistant to tigecycline. **Table 5** showed the MDR GN isolates. The most common MDR GN isolates were *A. baumannii* (40.4%), *K. pneumoniae* (19.4%), *P. aeruginosa* (16.3%). The penta-resistant bacteria constitutes approximately 23.2% of total MDR GN with *K. pneumoniae*, *E. coli* and *P. aeruginosa* as the most common penta-resistant organisms. The hepta-resistant bacteria constitute approximately 16.9% of total MDRGN bacteria with *K. pneumonia* and *P. aeruginosa* as the most common hepta-resistant bacteria. There were no MDR isolates.

Discussion. Most isolates were recovered from the respiratory specimens (38.8%) followed by the blood specimens (33%). These findings corroborated the results reported by other investigators from Italy and Finland.[17,18] The most common isolates observed in this study were *P. aeruginosa*, *A. baumannii*, *K. pneumoniae*, *S. aureus*, STACN, *E. coli*, *E. faecalis*, *E. faecium*, and *E. cloacae*. The most common GN bacilli included were *A. baumannii*, *P. aeruginosa*, *K. pneumoniae, E. coli, E. cloacae, S. marcescens,* and *S. maltophilia* making up to 62.1% of all isolates in the ICUs. This observation agreed with the finding of Lockhart et al,[19] that the most common GN bacilli reported to cause infections in the ICUs in the United States from 1993 to 2004 were *P. aeruginosa, E.coli, K. pneumoniae*, and *E. cloacae*. Several studies showed that *Acinetobacter spp*. and *P. aeruginosa* are the most common pathogens of ventilator-associated pneumonia (VAP), which agreed with the result of the current study that *Acinetobacter spp* and *P. aeruginosa* are the most common respiratory isolates.[20,21]

The most common GP cocci in this study were *S. aureus*, followed by STACN. Together both formed approximately 22% of the total isolates. These results agreed with the work of Fridkin et al[22] who studied the efficacy of hospital antibiograms in reflecting the pathogens resistance rates in hospital-acquired infections. They confirmed the efficacy of hospital antibiograms in reflecting the overall susceptibility patterns among isolates from hospital-acquired infections, however it underestimated the relative frequency of MRSA when associated with hospital-acquired infections. They explained this underestimation because of the reporting inaccuracy by the infection control practitioners responsible for reporting, as well as, due to the longer hospital stay of these patients, which exposed them to a higher risk for infection with antimicrobial-resistant pathogens.[22] On the other hand, Christianson et al[23] showed that MRSA made up 22.3% of all *Staphylococci* at ICUs in Canada.

The prevalence of VRE has increased globally since its emergence in the 1980's. In our study, 7.1% of *E. fecalis* and 40.1% of *E. faecium* were vancomycin-resistant. These results agreed with that obtained by Zhanel et al[24] who found that most of the VRE in North America in 2003 were of *E. faecium* (88%), while only 12% were of *E. faecalis*.[25] However, the difference in the percentage between our results and others may be due to the difference in the surveillance programs in hospitals that aim to prevent VRE colonization and bacteremia.[9] In this study, we found that ESBL producing *E. coli* were approximately 100% among the tested isolates, which were more common than that seen in *K. pneumoniae* (92%). However, the small size of the samples tested may give rise to biased results. All ESBL *E. coli* were MDR. We did not perform the genotype of ESBL *E. coli* to show their genetic relatedness. These results agreed with the results of Zhanel et al[9] who were the first to

document that ESBL-producing *E. coli* are becoming more common than ESBL-producing *Klebsiella spp*. This study highlighted the increased prevalence of antimicrobial resistant bacteria in ICU patients. Other studies showed that the bacterial resistance in patients treated at the ICU was higher than in patients in other parts of the hospital, such as medical/surgical wards, emergency rooms, and outpatient clinics.[17,19,26,27]

In this study, resistance rates for MRSA isolates were high for co-trimoxazole (46%), clindamycin (56%), fluoroquinolones (68%), as well as macrolides (85%), and lower with bacitracin (0%), chloramphenicol (7%), as well as rifampicin (17%). Thus, bacitracin and chloramphenicol still represent a reasonable empirical topical treatment for mild to moderate infections (such as, skin and soft tissue infections) caused by MRSA. However, serious side effects of chloramphenicol, such as bone marrow depression and aplastic anemia may hinder its use. These resistance rates are to some extent consistent with previous reports with some difference among individual antibiotics.[28] These differences may be due to the different sampling time, early or late, after admission. The different environment also may be another factor because of the unique features of the Riyadh environment as one of the most booming cities in the desert environment of the Arabian Peninsula, particularly rapid growth of population and extensive urbanization.

All MRSA and MRSE isolates were susceptible to vancomycin, linezolid, and muprocin, while no *Enterococcus spp*. proved to be resistant to tigecycline and linezolid including VRE *Enterococci*. Vancomycin-resistant-MRSA was not reported in this study. However, Whitener et al[29] reported in 2004, a case with vancomycin-resistant-MRSA, and stated that recent exposure by patients to vancomycin is not necessary for the development of vancomycin-resistant-MRSA strains. The lowest resistance rates in GN bacilli were to meropenem (except for *A. baumannii* and *P. aeruginosa*), and amikacin (except for *A. baumannii* and *S. maltophilia*) in this study. Being available only in in intravenous form, meropenem use is limited to the inpatients and usually reserved to severe cases. This is an important factor to minimize its abuse. The decreased incidence of GN bacterial resistance to aminoglycosides may be due to their decreased use due to ototoxicity and nephrotoxicity. This agrees with the work of Francetić et al[30] who found that the aminoglycoside cycling in 6 tertiary ICUs on the rates of sepsis had decreased the rate of aminoglycoside resistance patterns. On the other hand, the increased incidence of GN bacterial resistance to ciprofloxacin resistance, especially *A. baumannii* (92%), *Citrobacter* (56%), and *E. coli* (50%) may reflect the abuse of this type of quinolones' group of antibiotics as they can be given orally and are relatively safe. These findings are consistent with the data reported by Zhanel et al[9] who found increased resistance to fluoroquinolones. Their data showed that fluoroquinolones' resistance in *E. coli* was 21.1%, and in *P. aeruginosa* from 23.8-25.5%, which is lower than in our study.

When we considered MDR as resistance of microorganisms to 3 or more classes of antibiotics, we had a very high rate of MDR in the nosocomial infection acquired in this Riyadh GICU (*A. baumannii* [40%], *K. pneumoniae* [19%], and *P. aeruginosa* [16%]). The rate decreased dramatically, if we considered MDR as resistance of microorganisms to 5 or more classes of antibiotics (*K. pneumoniae* [9.1%], *P. aeruginosa* [3.8%]. and *A. baumannii* [2.2%]). The incidence of MDR in the current study is more than that observed in the study of Lockhart et al[19] carried out in the United States between 1993 and 2004, and the study of Zhanel et al[9] carried out in Canada between 2005 and 2006. The increased incidence of MDR among ICU patients may be due to reasons, such as prior antimicrobial use, inadequate antimicrobial therapy, and long antimicrobial exposures that exert antimicrobial pressures that lead to the emergence of resistance in a previously susceptible GN bacterium. Another factor is the easy exogenous acquisition of MDR, which may occur through patient-to-patient spread in a contaminated health care worker hands, or environmental surfaces.[2] Other factors that are associated with the development of MDR bacteria are male gender, underlying co-morbidity of ischemic heart disease (as in *A. baumannii*), and mechanical ventilation.[31] Strict isolation of patients infected with MDR microorganisms and judicial use of antibiotics should be emphasized in order to prevent the spread of MDR.[32] Involvement of an infectious diseases specialist may help to improve cure and minimize further resistance development.[17]

This single center study data may not reflect antibiotic susceptibility in KSA as a whole. As a consequence, a multi-site study is advised to compare and contrast findings from other hospitals. Another limitation is a lack of certainty that all clinical specimens represented active infection. All of the isolates may not represent actual infection from patients. In addition, we did not correlate the samples to admission date data for each patient/clinical specimen, so we were unable to provide a more accurate description of community versus nosocomial onset infection.

In conclusion, this study showed that *P. aeruginosa, A. baumannii, K. pneumoniae, E. coli, S. aureus* (MSSA and MRSA), and STACN are the most common isolates recovered from clinical specimens in the GICU

of RMH. Respiratory tract specimens represent nearly 39% of all the specimens collected in the ICU. The MDR phenotype is common with *A. baumannii*, and *K. pneumoniea* in the GICU of RMH. We therefore recommend local resistance surveillance studies to follow that may help to reduce the problem of increasing emergence and spread of antimicrobial-resistant pathogens among ICU patients, and to develop new suitable antibiotic treatment guidelines according to the infection patterns.

Acknowledgment. *The authors gratefully acknowledge all laboratory technical staff at the Riyadh Military Hospital who offered the great help in conducting this study.*

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