Frequency and antimicrobial susceptibility of Gram-negative bacteria isolated from 2 hospitals in Makkah, Saudi Arabia

Atif H. Asghar, MSc, PhD, *Hani S. Faidah,* MSc, PhD.

ABSTRACT

الأهداف : لتقييم مدى انتشار البكتريا السالبة الجرام ومقاومتها للمضادات الحيوية بمستشفيات مكة المكرمة – المملكة العربية السعودية .

الطريقة : أجريت الدراسة بمستشفى النور التخصصي ومستشفى حراء العام – مكة المكرمة – المملكة العربية السعودية خلال الفترة من شهر أكتوبر2005م إلى مارس 2006م . تم عزل عدد 1137 بكتريا سالبة الجرام (غير مكررة) من العينات الإكلينيكية بمختلف أجزاء الجسم لعدد 965 مريض . تم جمع المعلومات الدمغرافية، وأنواع البكتريا وحساسيتها للمضادات الحيوية من السجلات الطبية والمعملية للمرضى .

النتائج : أوضحت النتائج أن بكتريا (*Escherichia coli*) وبكتريا (*Pseudomonas aeruginosa*) أكثر الأنواع شيوعاً في البكتريا السالبة الجرام، حيث بلغت (31.6%) و (31.2%) على التوالي . ثم يلي ذلك بكتريا *Acinetobacter baumannii* ثم *Klebsiella pneumoniae*، ثم *Klebsiella sp*، ثم *Haemophilus influenzae*، ثم *Proteus sp* و *Enterobacter sp*. بلغت النسب على التوالي (10.8%، 8.3%، 6.2%، 3.7%، 3.3%، 1.9%) . كما أظهرت النتائج زيادة معدل مقاومة البكتريا السالبة الجرام للمضادات الحيوية المستعملة . وأيضا أظهرت الدراسة أن المقاومة المتعددة للمضادات الحيوية ضمن البكتريا السالبة الجرام يعتبر شائعاً في هذه الدراسة .

خاتمة : أتضح من خلال الدراسة أن هناك زيادة في معدل مقاومة البكتريا السالبة الجرام للمضادات الحيوية مقارنة بمناطق أخرى في دول العالم . إنّ تطبيق برامج المراقبة إجراء مهمُ في إستراتيجية التحكم في منع زيادة ظهور المقاومة للمضادات الحيوية لهذه النوع من البكتريا في المستشفيات .

Objectives: To estimate the prevalence and antibiotic susceptibility of the Gram-negative bacteria isolated from 2 hospitals in Makkah.

Methods: This study was undertaken in 2 main tertiary care hospitals namely; Al-Noor Specialist Hospital, and Hera Hospital in Makkah, Kingdom of Saudi Arabia from October 2005 to March 2006. A total of 1137 Gram-negative bacteria were identified in non-duplicate clinical specimens obtained from 965 patients of various body sites infections. Demographic data, identity of microorganisms, and antimicrobial susceptibilities were obtained from medical and laboratory records.

Results: The most prevalent Gram-negative bacteria were *Escherichia coli* (31.6%), and *Pseudomonas aeruginosa* (31.2%), followed by *Acinetobacter baumannii* (10.8%), *Klebsiella pneumoniae* (8.3%), *Klebsiella sp.* (6.2%), *Haemophilus influenzae* (3.7%), *Proteus sp.* (3.3%), and *Enterobacter sp.* (1.9%). Results demonstrated that Gram-negative bacteria have a high rate of resistance to commonly used antibiotics. Furthermore, multi-drug resistance was also common in this study.

Conclusion: Our data showed a high rate of resistance among Gram-negative pathogens in comparison with other countries in the world. The implementation of monitoring programs is an important part of the prevention strategy against the development of antibiotic resistance in hospitals.

Saudi Med J 2009; Vol. 30 (8): 1017-1023

From the Department of Environmental and Health Research (Asghar), The Custodian of the Two Holy Mosques Institute for Hajj Research, and the Department of Medical Microbiology (Faidah), Faculty of Medicine and Medical Sciences, Umm Al-Qura University, Makkah, Kingdom of Saudi Arabia.

Received 11th April 2009. Accepted 18th June 2009.

Address correspondence and reprint request to: Associate Professor Atif H. Asghar, Department of Environmental and Health Research, The Custodian of the Two Holy Mosques Institute for Hajj Research, Umm Al-Qura University, PO Box 6287, Makkah, Kingdom of Saudi Arabia. Tel. +966 505511003. Fax. +966 (2) 5573282. E-mail: ahasghar@uqu.edu.sa

Antimicrobial resistance is a major global problem in both developing and developed countries.[1] The emergence and spread of antimicrobial resistance has contributed to the morbidity, mortality, and increased health care costs resulting from treatment failures, and longer hospital stays.[2] Significant geographical variation was seen in antibiotic susceptibility, probably reflecting differences in infection control procedures, and the level of antibiotic use. Surveillance and monitoring programs are helpful for the development of empirical approaches for the treatment of serious infections, as well as, prevention and control of infections caused by resistant microorganisms.[3,4] Makkah is a city in the Kingdom of Saudi Arabia, and considered as the holiest city in Islam. Annually, Hajj pilgrimage attracts more than 2 million pilgrims to the city from 140 countries, in which many of the pilgrims are from the developing world, where particular diseases may be endemic. Moreover, approximately 10 million individuals visit Makkah all year round. This study aimed to estimate the prevalence, and antibiotic susceptibility of Gram-negative bacteria isolated from 2 hospitals in Makkah, Kingdom of Saudi Arabia.

Methods. This prospective study was undertaken in 2 main tertiary care hospitals in Makkah; Al-Noor Specialist Hospital (560 beds), and Hera Hospital (263 beds) during a period of 6 months from October 2005 to March 2006 (Ramadan 1426-Safar 1427 AH). A total of 1137 Gram-negative bacterial isolates were identified from 965 patients during the study period (only patients with completed data were included in the study). Demographic data (age, gender, nationality, type of infection, and ward of hospitalization) of patients with Gram-negative bacterial infection, and laboratory results of the clinical specimens of those patients (type of microorganisms, antimicrobial susceptibilities) were collected from the medical and laboratory records for each patient on a standardized collection form. During the study period, the isolates were collected from patients with different sites of infection, and identified using the standard routine microbiological methods including; morphology on culture media, gram-stained, and further identified using the API20E biochemical tests (Bio Merieux, Hazelwood, USA). Antimicrobial susceptibilities were performed in accordance with the Clinical and Laboratory Standard Institute (CLSI) guidelines. This study was approved by the local ethical committee in accordance with the Helsinki Declaration of 1975, as revised in 2000.

The results were statistically analyzed using the Statistical Package for Social Science software version 13 (SPSS Inc., Chicago, IL., USA). Descriptive statistical tests were presented as frequency and percentages.

Results. During the study period, a total of 1137 Gram-negative bacteria were identified in clinical specimens obtained from patients with various body site infections. The majority of Gram-negative bacteria were from Al-Noor Hospital (63%), of which 592 cases (52.1%) were male, and 545 (47.9%) female. The age of patients with Gram-negative infections ranged from infancy to more than 80 years old. Approximately, 6.9% of cases were children under one year old, and the incidence increased to 20-28% in the age groups ranging between 20 and 80 years (**Figure 1**). Respiratory tract infections (RTI) were the most common infections caused by Gram-negative pathogens representing 396 cases (34.8%), followed by urinary tract infections (UTI) (285 cases [25.1%]), wound infections (280 cases [24.6%]), genital infections (75 cases [6.6%]), and septicemia (54 cases [5%]). The most prevalent Gram-negative pathogens in this study were *Escherichia coli* (*E. coli*) (31.6%), and *Pseudomonas aeruginosa* (*P. aeruginosa*)

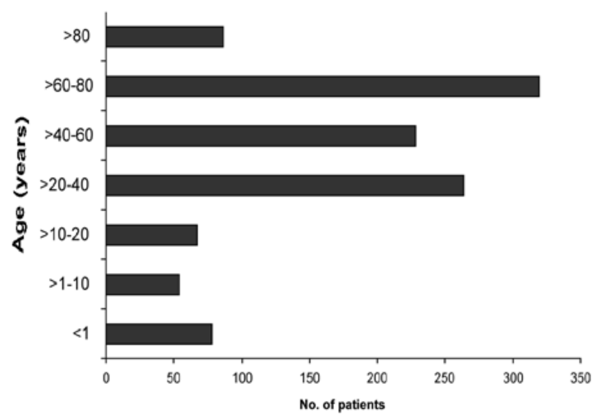

Figure 1 - Distribution of the Gram-negative infections according to patient age.

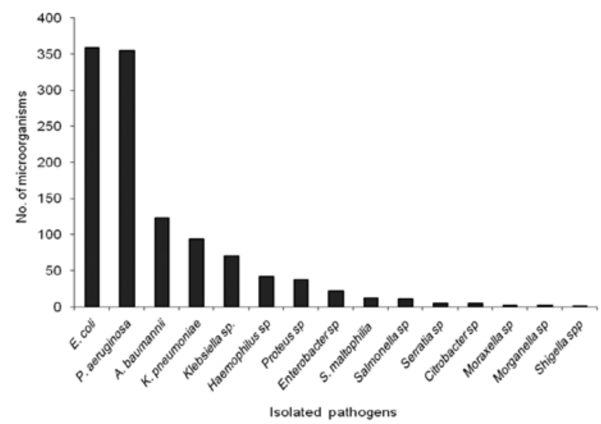

Figure 2 - Identified pathogens of the Gram-negative bacteria during the study period.

(31.2%), followed by *Acinetobacter baumannii* (*A. baumannii*) (10.8%), *Klebsiella pneumoniae* (*K. pneumoniae*) (8.3%), *Klebsiella sp.* (6.2%), *Haemophilus influenzae* (3.7%), *Proteus sp.* (3.3%), and *Enterobacter sp.* (1.9%) (**Figure 2**). Patients one year old and less were infected with a total of 81 Gram-negative pathogens in which *E. coli* was the most common isolated microorganism (42%) followed by *P. aeruginosa* (18.5%). On other hand, patients with age groups ranging from 41->80 were most commonly infected with *P. aeruginosa,* followed by *E. coli*, *A. baumannii*, and *K. pneumoniae* (**Table 1**). The male population was more often infected with *P. aeruginosa* representing 207 episodes out of 592 (35%) followed by *E. coli* (149 [25.2%]), and *A. baumannii* (81 [13.7%]). In contrast, *E. coli* was more predominant in the female population representing 210 out of 545 patients (38.5%), followed by *P. aeruginosa* (148 [27.2%]), and *K. pneumoniae* (46 [8.4%]). The distribution of Gram-negative pathogens by hospital wards is presented in **Table 2**. The *E. coli* and *P. aeruginosa* were the most common pathogens in most hospital wards. Most clinical isolates (329 out of 1137 isolates) were identified in the intensive care unit where *P. aeruginosa*, *E. coli*, and *A. baumannii* were the most predominant pathogens. According to bacterial species in relation to clinical infections, the results exhibited that, 396 cases with RTI were caused by 3 main bacterial pathogens; *P. aeruginosa*, *A. baumannii*, and *K. pneumoniae*. In cases with UTI, *E. coli* was the most frequently isolated, followed by *P. aeruginosa*, and *K. pneumoniae*. Similarly, *E. coli* and *P. aeruginosa* were the most common bacterial pathogens, causing wound infection. The *E. coli* was found mostly in patients with septicemia, and in female patients with genital

Table 1 - Frequency of Gram-negative pathogens according to patient's age groups.

Bacteria	<1 year	1-10 years	11-20 years	21-40 years	41-60 years	61-80 years	>80 years
	Freq (%)	Freq (%)	Freq (%)	Freq (%)	Freq (%)	Freq (%)	Freq (%)
Escherichia coli, n=359	34 (42)	17 (30.9)	21 (30.4)	99 (36)	70 (29.4)	92 (28)	26 (28.9)
Klebsiella pneumoniae, n=94	6 (7.4)	2 (3.6)	2 (2.9)	20 (7.2)	25 (10.5)	29 (8.8)	10 (11.1)
Klebsiella species, n=70	5 (6.2)	1 (1.8)	4 (5.8)	14 (5.1)	15 (6.3)	26 (7.9)	5 (5.6)
Pseudomonas aeruginosa, n=355	15 (18.5)	20 (36.4)	26 (37.7)	77 (28)	74 (31.1)	113 (34.4)	30 (33.3)
Acinetobacter baumannii, n=123	7 (8.6)	1 (1.8)	7 (10.1)	35 (12.7)	24 (10.1)	38 (11.5)	11 (12.2)
Proteus sp., n=37	2 (2.5)	3 (5.5)	5 (7.3)	6 (2.2)	4 (1.7)	13 (4)	4 (4.5)
Haemophilus influenzae, n=42	4 (4.9)	6 (10.9)	3 (4.4)	9 (3.3)	14 (5.9)	4 (1.2)	2 (2.2)
Enterobacter sp., n=22	3 (3.7)	1 (1.8)	0 (0)	9 (3.3)	5 (2.1)	3 (0.9)	1 (1.1)
Others, n=35	5 (6.2)	4 (7.3)	1 (1.4)	6 (2.2)	7 (2.9)	11 (3.3)	1 (1.1)
Total, n=1137	**81 (100)**	**55 (100)**	**69 (100)**	**275 (100)**	**238 (100)**	**329 (100)**	**90 (100)**

Others include: *Moraxella, Morganella, Salmonella, Shigella and Citrobacter species (sp)*, freq - frequency

Table 2 - Frequency of Gram-negative pathogens according to hospital wards.

Gram-negative pathogens	MSW	MMW	FSW	FMW	ICU	Pediatric	Obstetrics	Urology	OPD
	Freq. (%)	Freq. (%)	Freq. (%)	Freq. (%)	Freq. (%)	Freq. (%)	Freq. (%)	Freq. (%)	Freq. (%)
Escherichia coli, n=359	40 (11.1)	47 (13.1)	23 (6.4)	56 (15.6)	75 (20.9)	17 (4.7)	25 (7)	14 (3.9)	62 (17.3)
Pseudomonas aeruginosa, n=355	61 (17.2)	65 (18.3)	25 (7)	54 (15.2)	111 (31.3)	11 (3.2)	8 (2.3)	1 (0.3)	19 (5.4)
Acinetobacter baumannii, n=123	15 (12.2)	14 (11.4)	5 (4.1)	9 (7.3)	73 (59.3)	3 (2.4)	3 (2.4)	0 (0)	1 (0.8)
Klebsiella pneumoniae, n=94	8 (8.5)	20 (21.3)	9 (9.6)	15 (16)	20 (21.3)	1 (1.2)	1 (1.1)	2 (2.1)	18 (19.1)
Klebsiella sp., n=70	8 (11.4)	11 (15.7)	4 (5.7)	16 (22.9)	14 (20)	5 (7.1)	7 (10)	2 (2.9)	3 (4.3)
Haemophilus influenzae, n=42	1 (2.4)	11 (26.2)	0 (0)	5 (11.9)	15 (35.7)	7 (16.7)	3 (7.1)	0 (0)	0 (0)
Proteus sp., n=37	8 (21.6)	8 (21.6)	3 (8.1)	8 (21.6)	8 (21.6)	1 (2.7)	0 (0)	0 (0)	1 (2.7)
Enterobacter sp., n=22	5 (22.7)	3 (13.6)	5 (22.7)	2 (9.1)	3 (13.6)	1 (4.5)	2 (9.1)	0 (0)	1 (4.5)
Others, n=35	4 (11.4)	5 (14.3)	3 (8.6)	5 (14.3)	10 (28.6)	5 (14.3)	0 (0)	0 (0)	3 (8.6)
Total, n=1137	**150**	**184**	**77**	**170**	**329**	**51**	**49**	**19**	**108**

MSW - male surgical ward, MMW - male medical ward, FSW - female surgical ward, FMW - female medical ward, ICU -intensive care unit, OPD - out-patient department, Others include: *Moraxella, Morganella, Salmonella, Shigella and Citrobacter species (sp),* freq - frequency

Table 3 - Distribution of Gram-negative pathogens according to the site of infection.

Gram-negative pathogens	Infections											
	UTI		RTI		Wound infection		Septicemia		Female genital infection		Other infections	
	Frequency (%)											
Escherichia coli, n=359	162	(56.8)	38	(9.6)	96	(34.3)	19	(35.2)	40	(53.3)	4	(8.5)
Pseudomonas aeruginosa, n=355	46	(16.1)	169	(42.7)	96	(34.3)	16	(29.6)	11	(14.7)	17	(36.2)
Acinetobacter baumannii, n=123	8	(2.8)	78	(19.7)	24	(8.6)	7	(13)	5	(6.6)	1	(2.1)
Klebsiella pneumoniae, n=94	27	(9.5)	39	(9.9)	17	(6.1)	6	(11.1)	3	(4)	2	(4.3)
Klebsiella sp., n=70	21	(7.4)	17	(4.3)	15	(5.4)	3	(5.5)	10	(13.3)	4	(8.5)
Haemophilus influenzae, n=42	0	(0)	33	(8.3)	1	(0.4)	1	(1.9)	4	(5.3)	3	(3.4)
Proteus sp., n=37	9	(3.2)	6	(1.5)	20	(7.1)	0	(0)	0	(0)	2	(4.3)
Enterobacter sp., n=22	10	(3.5)	3	(0.8)	6	(2.1)	1	(1.9)	1	(1.3)	1	(2.1)
Others, n=35	2	(0.7)	13	(3.3)	5	(1.8)	1	(1.9)	2	(2.6)	13	(27.7)
Total, n=1137	**285**	**(100)**	**396**	**(100)**	**280**	**(100)**	**54**	**(100)**	**75**	**(100)**	**47**	**(100)**

Table 4 - Antimicrobial resistance among Gram-negative isolates.

Antibiotic class	Antibiotics (μg)	*E. coli*		*K. pneumoniae*		*Klebsiella sp.*		*P. aeruginosa*		*A. baumannii*		*Proteus sp.*		*H. influenzae*		*Enterobacter sp.*	
		n (%)															
Cephalosporins	Cephalothin (30)	286	58.4	73	38.4	38	36.8	25	76	56	100	24	33.3	27	40.7	15	100
	Cefoxitin (30)	327	11.6	77	15.6	63	19	37	73	96	97.9	32	15.6	37	10.8	20	90
	Cefuroxime (30)	47	36.2	8	37.5	5	60	4	-	1	100	7	28.6	2	-	1	100
	Ceftazidime (30)	252	24.6	68	32.4	54	31.5	296	52.7	99	86.9	29	6.9	17	-	13	46.2
	Cefotaxime (30)	132	15.2	31	22.6	9	33.3	19	-	12	83.3	9	33.3	2	-	2	-
	Cefotriaxone (30)	149	18.8	48	22.9	19	42.1	92	82.6	30	96.7	9	-	7	-	9	55.6
Other β-lactam	Ampicillin (10)	336	83.9	85	95.3	65	98.5	37	70.3	97	96.9	36	52.8	40	40	21	95.2
	Aztreonam (30)	209	30.1	50	34	59	37.3	309	57.6	106	95.3	34	11.8	16	12.5	15	46.7
	Piperacillin (100)	194	59.3	48	54.2	55	43.6	322	49.4			31	19.4	17	23.5	12	50
	Piperacillin/ Tazobactam (110)	148	8.8	31	9.7	28	7.1	161	33.5	47	42.6	3	33.3	10	-	10	20
	Amoxicillin/CA (30)	318	51.6	82	29.3	57	43.9	34	76.5	85	92.9	28	32.1	36	8.3	19	100
	Imipenem (10)	74	8.1	11	9.1	34	8.8	135	38.5	61	45.9	17	5.9	11	-	5	-
	Meropenem (10)	154	1.3	-	-	9	-	106	19.8	25	28	7	-	-	-	3	-
	Imipenem/CS (10)	126	2.4	20	5	52	-	221	25.3	81	14.8	26	7.7	13	-	12	-
Amino-glycosides	Amikacin (30)	236	11.4	67	10.4	52	21.2	339	48.1	101	84.2	33	27.3	18	44.4	13	7.7
	Gentamicin (10)	316	25.9	83	25.3	59	32.2	234	50.4	101	76.2	30	43.3	37	32.4	18	38.9
	Tobramycin (10)	63	22.2	15	20	11	36.4	59	54.2	23	56.5	7	85.7	4	50	3	66.7
Fluoro-quinolones	Ciprofloxacin (5)	195	45.6	54	31.5	53	34	279	50.9	-	-	30	16.7	15	-	11	9.1
	Levofloxacin	40	52.5	4	50	2	50	16	75	11	63.6	6	50	5	-	2	-
	Norfloxacin (10)	105	32.4	23	39.1	9	55.6	162	58	66	71.2	24	4.2	10	10	9	33.3
	Nalidixic acid (30)	145	49	26	42.3	19	47.4	23	95.7	6	33.3	5	80			7	57.1
	Norfl. /Ciprof.	46	39.1	9	33.3	7	57.1	27	44.4	-	-	4	-	1	-	3	66.7
Others	Tetracycline (30)	41	56.1	7	85.7	6	66.7	99	72.7	-	-		100	-	-	1	-
	Cotrimoxazole (25)	311	58.8	85	36.5	62	51.6	39	76.9	69	75.4	21	66.7	31	67.7	17	23.5
	Nitrofurantoin (30)	179	11.7	34	26.5	19	31.6	26	96.2	6	83.3	12	66.7	-	-	7	28.6

E. coli - Escherichia coli, K. pneumoniae - Klebsiella pneumoniae, P. aeruginosa - Pseudomonas aeruginosa, A. baumannii - Acinetobacter baumannii, H. influenzae - Haemophilus influenzae, Norfl/Ciprof - Norfloxacin/Ciprofloxacin infection (**Table 3**). The most common infection in the ICU patients was RTI, which represents 179 out of 329 (54.4%). However, wound infections were the highest infection in the surgical ward for both genders in comparison with other hospital wards. Regarding the pediatric ward, UTI, and RTI were the major bacterial infections found (data not shown). Antimicrobial susceptibility for selected antimicrobial agents against isolated Gram-negative pathogens is shown in **Table 4**. Overall, susceptibility rates for *E. coli* strains were high in this study for most tested antimicrobial agents. High resistance rates were observed in cephalothin (58.4%), ampicillin (83.9%), piperacillin (59.3%), amoxicillin/clavulanic acid (51.6%), cotrimoxazole (58.8%), levofloxacin (52.5%), nalidixic acid (49%), tetracycline (56.1%), and ciprofloxacin (45.6%). On other hand, *E. coli* isolates showed a very low resistance rate to meropenem, imipenem/ cilastatin sodium (CS), and imipenem. The *K. pneumoniae* isolates showed moderate resistance (15-40%) to most antibiotics, while a high resistance rate were seen to ampicillin, piperacillin, levofloxacin, and nalidixic acid. The *K. pneumoniae* isolates showed a low resistance rate to imipenem/CS, imipenem, piperacillin/tazobactam, and amikacin. Regarding *Klebsiella sp.*, the results exhibit a similar resistance rate to some antibiotics as *K. pneumoniae*. A large proportion of *P. aeruginosa* showed a high rate of resistance ranging from 50-90% to ß-lactams, aminoglycosides, and fluoroquinolones. In contrast, moderate resistance *P. aeruginosa* isolates was observed to imipenem, imipenem/CS, and meropenem. The *A. baumannii* showed high resistance to most antimicrobial agents ranging from 50-100%. Moderate resistance rates (15-40%) were found to imipenem, piperacillin/tazobactam, meropenem, nalidixic acid, and imipenem/CS.

Discussion. The results demonstrated that a total of 1137 Gram-negative bacteria were identified during the 6 months study. Fifteen Gram-negative bacterial species was identified to cause infections throughout the study period. Generally, *E. coli* (31.6%), and *P. aeruginosa* (31.2%) were the main pathogens isolated in the hospitals under this study. Many international studies reported that *P. aeruginosa* was the most frequently isolated Gram-negative bacteria in comparison to *E. coli,* and other bacterial isolates.[5-8] This difference in the frequency of the type of bacterial isolates between hospitals is most probably due to the variation in patient populations, departments in each hospital, and subsequently the type of specimens sent to laboratories.

The majority of Gram-negative bacteria in this study originated from RTI, followed by UTI, and wound infections. The main pathogens isolated from the respiratory tract were *P. aeruginosa* (42.7%), *A. baumannii* (19.7%) and *K. pneumoniae* (9.6%). A previous study in Latin America showed that *P. aeruginosa* was the most prevalent pathogen causing pneumonia monitored by the SENTRY Program, and *Acinetobacter sp.* was encountered among the top 5 pathogens causing RTI.[9] Urinary tract infections were also common in this study. Although, the isolated pathogens from patients with UTI are similar to those species isolated in many regions of the world, the rank order of pathogens occurrence was different in these studies.[10-12] In this study, the main pathogens involved in UTI were *E. coli* (56.8%) followed by *Klebsiella sp.* (including *K. pneumoniae*) (16.8%) and *P. aeruginosa* (16.1%). Similar rank order for pathogens causing UTI was found in a study of the Asia-Western Pacific region: 37.8% for *E. coli*, 12.3% for *Klebsiella sp.*, and 11.1% for *P. aeruginosa*.[10] A study in Spain showed that UTI was caused by *E. coli* in 47% of the cases, which is in agreement with our results.[13] The high prevalence of Gram-negative non-fermentative bacilli and *Enterobacteriaceae* in this study may indicate that the majority of our isolates originated from patients with nosocomial infections. It has been reported that the incidence of nosocomial infections in the ICU is 2-5 times greater than in the general inpatient population, predominantly due to RTI (pneumonia), and UTI.[14]

Many factors contribute to the increasing risk of nosocomial infections and antimicrobial resistance in the ICU which includes; the growing complexity of the ICU, the impaired host defenses of patients, invasive monitoring and procedures, exposure to multiple antibiotics, and colonization by resistant microorganisms.[14,15] In agreement with other international studies, our results showed that most bacterial pathogens were isolated from the ICU patients, and most of these pathogens were *P. aeruginosa*, *E. coli*, and *A. baumannii*.[16,17] Regarding *Acinetobacter* nosocomial infection, it was reported that the lower respiratory tract is the most common site to isolate this microorganism, especially in mechanically ventilated patients, where *Acinetobacter sp*. has been recognized as a typical pathogen in late-onset ventilator-associated pneumonia.[18]

In general, the results demonstrated that gram-negative bacteria have high rates of resistance to commonly used antibiotics. The *E. coli* clinical isolates still showed a high susceptibility to meropenem, imipenem/ CS, and imipenem, and *K. pneumoniae* showed a high susceptibility to imipenem/CS, imipenem, piperacillin/ tazobactam, and amikacin. It was reported that the susceptibility of *Enterobacteriaceae* to the carbapenems was unaffected by the production of extended-spectrum beta-lactamase, or AmpC β-lactamases.[19] This could make the rate of resistance among *Enterobacteriaceae* against carbapenems very limited. On the other hand, *P. aeruginosa* and *A. baumannii* showed high rates of resistance ranging from 50-100% to most antimicrobial agents. Moderate resistance rates were found among carbapenems ranging from 25-46%. The rates of antimicrobial resistance found in this work were much higher than those published in developed countries, but were similar or lower to those reported in developing countries.[16,20]

In agreement to other international studies, our results indicated that, carbapenems are still the antibiotics of choice to most Gram-negative bacilli.[19] Multi-drug resistance (MDR) among Gram-negative isolates was also common in this study. The MDR among *P. aeruginosa* was defined as resistance to at least 3 of the 4 drugs; ceftazedime, imipenem, ciprofloxacin, and tobramycin.[21] According to this definition, the results indicated that approximately 50% of *P. aeruginosa* clinical isolates were MDR. This result is higher than that previously reported in the United States (37%).[21] The *A. baumannii* isolates were resistant to most used antibiotics. Similarly, many studies in the United States, Brazil, and Europe have shown the presence of MDR among *A. baumannii*.[20,22,23]

In conclusion, expansion of resistance to antimicrobial agents is currently the main concern of the medical community worldwide, since infections caused by resistant bacterial strains seem to be associated with worsened morbidity factors (hospitalization, death, and illness rates). Our data showed a high rate of resistance among Gram-negative pathogens, and resistance to carbapenems is still rare in this area among *E. coli*, *K. pneumoniae*, and other *Klebsiella* species. However, *P. aeruginosa* and *A. baumannii* have shown to be a rising problem in Makkah, due to its prevalence and resistance patterns. Generally, many factors might have contributed and leads to increased rates of antimicrobial resistance. These factors include misuse of antibiotics by health professionals, unskilled practitioners and laypersons, misuse of antibiotics by the public, poor drug quality, unhygienic conditions accounting for the spread of resistant bacteria, and inadequate surveillance.[3]

This study being conducted on 2 hospitals in Makkah is not representative of the general population of Saudi Arabia, and this had limited our study. Further studies with the addition of a national project is recommended to evaluate antimicrobial susceptibility of Gram-negative bacteria isolated from hospitals and health centers in the different region of Saudi Arabia. Moreover, detection of resistance mechanism of these organisms is useful for the geographical distribution worldwide.

Acknowledgment. *The authors gratefully acknowledge Dr. Osamah F. Al-Bar (former Dean of the Custodian of the Two Holy Mosques Institute of Hajj Research) for his help and support. We thank Mr. Faisal O. Menshawi, Mr. Radi T. Al-Safi, Mr. Fadi S. Qashqari and Mr. Sharaf E. Sharaf (Medical Sciences students) for their help in specimen collection and practical assistance. We would like also to thank all the hospital staff (from Al-Noor Specialist Hospital, and Hera Hospital) involved in this study, for without their help this work would not have been possible.*

References

1. Lauderdale TL, Clifford McDonald L, Shiau YR, Chen PC, Wang HY, Lai JF, et al. The status of antimicrobial resistance in Taiwan among gram-negative pathogens: the Taiwan surveillance of antimicrobial resistance (TSAR) program, 2000. ***Diagn Microbiol Infect Dis*** 2004; 48: 211-219.
2. Maragakis LL, Perencevich EN, Cosgrove SE. Clinical and economic burden of antimicrobial resistance. ***Expert Rev Anti Infect Ther*** 2008; 6: 751-763.
3. Deasy J. The antibiotic challenge: changing clinical management of infections. ***JAAPA*** 2009; 22: 22-26.
4. Nicolau DP. Management of complicated infections in the era of antimicrobial resistance: the role of tigecycline. ***Expert Opin Pharmacother*** 2009: 10: 1213-1222.
5. Kiffer C, Hsiung A, Oplustil C, Sampaio J, Sakagami E, Turner P, et al. Antimicrobial susceptibility of Gram-negative bacteria in Brazilian hospitals: the MYSTIC Program Brazil 2003. ***Braz J Infect Dis*** 2005; 9: 216-224.
6. Makedou KG, Tsiakiri EP, Bisiklis AG, Chatzidimitriou M, Halvantzis AA, Ntoutsou K, et al. Changes in antibiotic resistance of the most common Gram-negative bacteria isolated in intensive care units. ***J Hosp Infect*** 2005; 60: 245-248.
7. Wang H, Chen M; China Nosocomial Pathogens Resistance Surveillance Study Group. Surveillance for antimicrobial resistance among clinical isolates of gram-negative bacteria from intensive care unit patients in China, 1996 to 2002. ***Diagn Microbiol Infect Dis*** 2005; 51: 201-208.
8. Yang QW, Xu YC, Chen MJ, Hu YJ, Ni YX, Sun JY, et al. [Surveillance of antimicrobial resistance among nosocomial gram-negative pathogens from 15 teaching hospitals in China in 2005] ***Zhonghua Yi Xue Za Zhi*** 2007; 87: 2753-2758. Chinese.
9. Gales AC, Sader HHS, Jones RN. Respiratory tract pathogens isolated from patients hospitalized with suspected pneumonia in Latin America: frequency of occurrence and antimicrobial susceptibility profile: results from the SENTRY Antimicrobial Surveillance Program (1997-2000). ***Diagn Microbiol Infect Dis*** 2002; 44: 301-311.
10. Bell JM, Turnidge JD, Gales AC, Pfaller MA, Jones RN; Sentry APAC Study Group. Prevalence of extended spectrum beta-lactamase (ESBL)-producing clinical isolates in the Asia-Pacific region and South Africa: regional results from SENTRY Antimicrobial Surveillance Program (1998-99). ***Diagn Microbiol Infect Dis*** 2002; 42: 193-198.
11. Gales AC, Sader HS, Jones RN; SENTRY Participants Group (Latin America Urinary tract infection trends in Latin American hospitals: report from the SENTRY antimicrobial surveillance program (1997-2000). ***Diagn Microbiol Infect Dis*** 2002; 44: 289-299.

12. Jones RN, Kugler KC, Pfaller MA, Winokur PL. Characteristics of pathogens causing urinary tract infections in hospitals in North America: results from the SENTRY Antimicrobial Surveillance Program, 1997. ***Diagn Microbiol Infect Dis*** 1999; 35: 55-63.
13. Daza R, Gutiérrez J, Piédrola G. Antibiotic susceptibility of bacterial strains isolated from patients with community-acquired urinary tract infections. ***Int J Antimicrob Agents*** 2001; 18: 211-215.
14. Meric M, Willke A, Caglayan C, Toker K. Intensive care unit-acquired infections: incidence, risk factors and associated mortality in a Turkish university hospital. ***Jpn J Infect Dis*** 2005; 58: 297-302.
15. Sligl W, Taylor G, Brindley PG. Five years of nosocomial Gram-negative bacteremia in a general intensive care unit: epidemiology, antimicrobial susceptibility patterns, and outcomes. ***Int J Infect Dis*** 2006; 10: 320-325.
16. Zarakolu P, Hasçelik G, Unal S. [Antimicrobial susceptibility pattern of nosocomial gram negative pathogens: results from MYSTIC study in Hacettepe University Adult Hospital (2000-2004)] ***Mikrobiyol Bul*** 2006; 40: 147-154. Turkish.
17. Streit JM, Jones RN, Sader HS, Fritsche TR. Assessment of pathogen occurrences and resistance profiles among infected patients in the intensive care unit: report from the SENTRY Antimicrobial Surveillance Program (North America, 2001). ***Int J Antimicrob Agents*** 2004; 24: 111-118.
18. Young LS, Sabel AL, Price CS. Epidemiologic, clinical, and economic evaluation of an outbreak of clonal multidrug-resistant Acinetobacter baumannii infection in a surgical intensive care unit. ***Infect Control Hosp Epidemiol*** 2007; 28: 1247-1254.
19. Turner PJ. Extended-spectrum beta-lactamases. ***Clin Infect Dis*** 2005; 41 (Suppl 4): S273-S275.
20. Rhomberg PR, Fritsche TR, Sader HS, Jones RN. Clonal occurrences of multidrug-resistant Gram-negative bacilli: report from the Meropenem Yearly Susceptibility Test Information Collection Surveillance Program in the United States (2004). ***Diagn Microbiol Infect Dis*** 2006; 54: 249-257.
21. Jung R, Fish DN, Obritsch MD, MacLaren R. Surveillance of multi-drug resistant Pseudomonas aeruginosa in an urban tertiary-care teaching hospital. ***J Hosp Infect*** 2004; 57: 105-111.
22. Gales AC, Pfaller MA, Sader HS, Hollis RJ, Jones RN. Genotypic characterization of carbapenem-nonsusceptible Acinetobacter spp. isolated in Latin America. ***Microb Drug Resist*** 2004; 10: 286-291.
23. Van Looveren M, Goossens H; ARPAC Steering Group. Antimicrobial resistance of Acinetobacter spp. in Europe. ***Clin Microbiol Infect*** 2004; 10: 684-704.

Related topics

Mashouf RY, Zamani A, Farahani HS. Diagnostic multiplex polymerase chain reaction assay for the identification of *Pseudomonas aeruginosa* from the skin biopsy specimens in burn wound infections and detection of antibiotic susceptibility. ***Saudi Med J*** 2008; 29: 1109-1114.

Aslani MM, Ahrabi SS, Alikhani YM, Jafari F, Zali RM, Mani M. Molecular detection and antimicrobial resistance of diarrheagenic *Escherichia coli* strains isolated from diarrheal cases. ***Saudi Med J*** 2008; 29: 388-392.

Karima TM, Bukhari SZ, Ghais MA, Fatani MI, Hussain WM. Prevalence of *Helicobacter pylori* infection in patients with peptic ulcer diseases. ***Saudi Med J*** 2006; 27: 621-626.

Ozgunes I, Erben N, Kiremitci A, Kartal ED, Durmaz G, Colak H, Usluer G, Colak E. The prevalence of extended-spectrum beta lactamase-producing Escherichia coli and Klebsiella pneumoniae in clinical isolates and risk factors. ***Saudi Med J*** 2006; 27: 608-612.

Kader AA, Angamuthu K. Extended-spectrum beta-lactamases in urinary isolates of *Escherichia coli, Klebsiella pneumoniae* and other gram-negative bacteria in a hospital in Eastern Province, Saudi Arabia. ***Saudi Med J*** 2005; 26: 956-959.

Al-Jasser AM, Elkhizzi NA.Antimicrobial susceptibility pattern of clinical isolates of *Pseudomonas aeruginosa*. ***Saudi Med J*** 2004; 25: 780-784.