



## ORIGINAL ARTICLE

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# Antibiotic Resistance Trends of Gram-negative Bacteria Most Frequently Isolated from Inpatients in a Tertiary Care Hospital in Sana'a, Yemen

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## ABSTRACT

**Objectives:** To determine the trends of antibiotic resistance of Gram-negative bacteria most frequently isolated from inpatients at the University of Science and Technology Hospital (USTH) in Sana'a, Yemen.

**Methods:** A retrospective, cross-sectional study on the antibiotic resistance of Gram-negative bacteria most frequently isolated from respiratory tract, pus, urine, blood and other types of specimens from inpatients admitted to the USTH. Data were retrieved from the hospital records of culture-positive inpatients in the period from January 2006 to December 2013, and annual trends of resistance were compared using chi-square test for trends at  $P$  values  $< 0.05$ .

**Results:** Of 2005 Gram-negative bacterial isolates in the period from 2006 to 2013, the most frequently isolated species were *Escherichia coli* (41.6%), *Acinetobacter* species (26.7%), *Klebsiella* species (21.0%) and *Pseudomonas aeruginosa* (10.6%). Amikacin and carbapenems were the most active drugs against *E. coli*, with a decrease in the susceptibility of this species to the third- and fourth-generation cephalosporins and a variable resistance rate to quinolones that significantly increased in 2013. *Acinetobacter* species susceptibility to most antibiotics decreased significantly over the years of the study, where polymyxin B was the only one found to be effective against this species. On the other hand, the trend of *Klebsiella* species resistance to imipenem, piperacillin-tazobactam, cefepime, ceftazidime increased over the years of the study. Susceptibility of *Klebsiella* species to ciprofloxacin, levofloxacin and moxifloxacin showed fluctuations, while the susceptibility of aminoglycosides (amikacin and gentamicin) and ampicillin-sulbactam showed no difference. The resistance of *P. aeruginosa* to the majority of antibiotics was not dramatically changed over the years of the study period, but gentamicin resistance rate was considerably dropped from 77.8% in 2008 to 25.9% in 2013.

**Conclusions:** Of the most frequently isolated Gram-negative bacteria in Sana'a, *Acinetobacter* species have the highest resistance rate to the most commonly used antibiotics, where only polymyxin B is effective against this species. *P. aeruginosa* shows an unchanging rate of resistance to antibiotics in the USTH despite being quite resistant to antibiotics on a global scale, which could be attributed to the smaller number of *P. aeruginosa* isolates tested over the study period. Further large-scale studies on the trends of antibiotic resistance rates in hospital-based settings and the best ways to counteract such resistance in Yemen are recommended.

**Keywords:** Antibiotic resistance, Gram-negative bacteria, Inpatient, Hospital, Sana'a

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## 1. Introduction

Resistance of bacteria to antibiotics is usually caused by genetic modifications as a result of the irrational use of antibiotics. Gram-negative bacteria are one of the most common causes of infections in clinical settings (1, 2). They cause at least 30% of hospital-acquired infections and about 15-20% of meningitis in adults (3, 4). In the United States, Gram-negative bacteria cause about 70% of infections in intensive care units (ICUs). Furthermore, they are the most common cause of bloodstream infections, lower respiratory tract infections and urinary tract infections in ICUs (5-8). Decreased susceptibility of Gram-negative bacteria to commonly used antibiotics poses serious threats to the public health, leading to an increase in medical care cost, prolonged hospital length of stay, treatment failure and death (9-12). For example, in the United States, more than 23,000 deaths per year have been attributed to infections by antibiotic-resistant bacteria. In addition, the overall cost resulting from antibiotic resistance has been estimated to be \$20 billion a year for healthcare costs and up to \$35 billion a year for the society (13).

In addition to the health and economic consequences of antibiotic resistance, a few new antimicrobials have been developed and approved over the past three decades, limiting the options to treat antibiotic-resistant bacteria (13, 14). The decline in the development of antibiotics is due to several factors, including the high cost required for drug development, relatively low rate of return on investment in antibiotics, challenges to screening for new compounds, decreased antibiotic longevity as a result of resistance emergence and unavailability of formal guidelines to evaluate antibiotic effectiveness and safety issues of new antimicrobial drugs (15-19).

Variations in antibiotic resistance among different institutions and countries highlight the importance of the localized antibiotic re-

sistance data in choosing the most appropriate empirical therapy for nosocomial infections (20). In Yemen, data on antibiotic resistance are very limited, particularly among inpatients. Therefore, the aim of the present study was to determine the trends to antibiotic resistance of Gram-negative bacteria most frequently isolated from inpatients admitted to the University of Science and Technology Hospital (USTH) in Sana'a city, Yemen.

## 2. Methods

### 2.1. Study design and setting

This retrospective, cross-sectional study was conducted in the USTH, a private tertiary care hospital with a 200-bed capacity. Inpatient departments included in the study were medical and surgical wards (for males and females), ICUs, and Coronary Care Unit.

### 2.2. Data collection

Data were retrieved from the hospital records of culture-positive inpatients admitted to the USTH in the period from January 01, 2006 to December 31, 2013. Only positive culture results of sputum, pus, urine, blood, wound, and other specimens for Gram-negative bacteria, which were isolated from patients older than 18 years and underwent standard cultivation and biochemical as well as antibiotic susceptibility testing, were included in this study. Data were collected on the susceptibility of bacterial isolates to the following antibiotics: imipenem, meropenem, piperacillin-tazobactam, cefepime, ceftazidime, ciprofloxacin, levofloxacin, moxifloxacin, amikacin, gentamicin, ampicillin-sulbactam, cefoperazone-sulbactam, and polymyxin (HIMEDIA Laboratories, Mumbai, India).

### 2.3. Data analysis

Antibiotic resistance of Gram-negative bacteria was presented as percentages of the total number of isolates per year. Data were analyzed using IBM SPSS Statistics for Windows, version 20.0 (IBM



Corp., Armonk, NY, USA), where annual trends of resistance were compared using chi-square test for trends. Differences at P values < 0.05 were considered to be statistically significant.

### 3. Results

Table (1) shows that of 2005 Gram-negative bacterial isolates in the period from 2006 to 2013, the most frequently isolated species were *Escherichia coli* (41.6%), *Acinetobacter* species (26.7%), *Klebsiella* species (21.0%) and *Pseudomonas aeruginosa* (10.6%). Regarding the origin of Gram-negative isolates, Table (2) shows that respiratory tract specimens (31.8%), pus (19.7%), urine (17.3%) and blood (14.2%) were the most frequent sources of the isolates. *E. coli* was most frequently isolated from urine (72.1%; 251/348), pus (58.5%; 231/395) and blood (42.1%; 120/285), while *Acinetobacter* species was most frequently isolated from respiratory tract specimens (47.9%; 305/637). Respiratory tract specimens, pus and blood were the most common sources for *Klebsiella* species, while *P. aeruginosa* was most frequently isolated from respiratory tract and pus specimens (Table 2).

#### 3.1. Resistance pattern of *E.coli*

Amikacin and carbapenems were the most active drugs against *E. coli* (Table 3). For extended-spectrum penicillin, the susceptibility of *E. coli* was good until 2012, but resistance rate reached to 27.5% in 2013. A decrease in the susceptibility to the third- and fourth-generation cephalosporins was also observed for *E. coli*. The resistance rate of *E. coli* to quinolones was variable, but it significantly increased in 2013 ( $p < 0.001$ ) (Table 3).

#### 3.2. Resistance pattern of *Acinetobacter* species

The susceptibility of *Acinetobacter* species to most antibiotics decreased significantly over the years of the study (Table 4). Although no

significant difference was found in the resistance rate of *Acinetobacter* species to meropenem ( $p = 0.061$ ) and gentamicin ( $p = 0.774$ ), both did not show an acceptable activity over the years of the study. Of all tested antibiotics, polymyxin B was the only one found to be effective against *Acinetobacter* species (Table 4).

#### 3.3. Resistance pattern of *Klebsiella* species

The trend in the resistance of *Klebsiella* species to imipenem ( $p < 0.001$ ), piperacillin-tazobactam ( $p < 0.001$ ), cefepime ( $p = 0.004$ ), ceftazidime ( $p = 0.007$ ) increased over the years of the study period (Table 5). Susceptibility to ciprofloxacin, levofloxacin and moxifloxacin showed fluctuations, while the susceptibility of aminoglycosides (amikacin and gentamicin) and ampicillin-sulbactam showed no difference ( $p = 0.151$ ), ( $p = 0.062$ ) and ( $p = 0.359$ ) respectively.

#### 3.4. Resistance pattern of *P. aeruginosa*

The resistance of *P. aeruginosa* was not dramatically changed to the majority of antibiotics over the years of the study period (Table 6). Nevertheless, gentamicin resistance rate was considerably dropped from 77.8% in 2008 to 25.9% in 2013 ( $p = 0.004$ ).

## 4. Discussion

Gram-negative bacteria were most frequently isolated from respiratory tract specimens of inpatients admitted to the USTH followed by those isolated from pus, urine, and blood. In contrast, other epidemiological studies elsewhere reported urine as the most frequent source of Gram-negative bacteria, with a variability in the distribution pattern of Gram-negative bacteria in other specimens such as blood, wound and sputum (1, 21-23). It is to be noted that the variability in the most frequent sources of Gram-negative bacteria among different institutions and countries is expected.



**Table 1.** Gram-negative bacterial isolates from inpatients in the USTH, Sana'a (2006–2013)

Isolated bacteria	Number of isolates								Total n (%)
	2006	2007	2008	2009	2010	2011	2012	2013	
<i>E. coli</i>	44	67	69	117	105	128	164	140	834 (41.6)
<i>Acinetobacter</i> species	1	6	42	115	95	98	82	97	536 (26.7)
<i>Klebsiella</i> species	18	33	30	39	57	52	115	78	422 (21.0)
<i>P. aeruginosa</i>	5	19	13	31	40	34	40	31	213 (10.6)
<b>Total</b>	68	125	154	302	297	312	401	346	2005

**Table 2.** Frequency of Gram-negative bacteria isolated from different clinical samples from inpatients admitted to the USTH, Sana'a (2006– 2013)

Type of sample	Bacterial species	Frequency of isolates per year								Total n (%)
		2006	2007	2008	2009	2010	2011	2012	2013	
Respiratory tract specimens*	<i>E. coli</i>	3 (20.0)	3 (11.5)	8 (17.0)	12 (13.8)	15 (13.0)	9 (9.5)	22 (17.5)	25 (19.8)	97 (15.2)
	<i>Klebsiella</i> species	10 (66.6)	14 (53.8)	13 (27.7)	19 (21.8)	28 (24.3)	19 (20.0)	37 (29.4)	27(21.4)	167 (26.2)
	<i>P. aeruginosa</i>	1 (6.6)	8 (30.7)	5 (10.6)	7 (8.0)	16 (13.9)	14 (14.7)	8 (6.3)	9 (7.1)	68 (10.7)
	<i>Acinetobacter</i> species	1 (6.6)	1 (3.8)	21 (44.7)	49 (56.3)	56 (48.7)	53 (55.8)	59 (46.8)	65 (51.6)	305 (47.9)
	<b>Total</b>	15 (2.4)	26 (4.1)	47 (7.3)	87 (13.6)	115 (18.0)	95 (15.0)	126 (19.8)	126 (19.8)	637 (100.0)
Pus#	<i>E. coli</i>	8(88.9)	16 (59.6)	13 (72.2)	28 (66.7)	16 (37.2)	48 (57.8)	66(57.8)	36 (57.1)	231 (58.5)
	<i>Klebsiella</i> species	0 (0.0)	4 (17.4)	0 (0.0)	3 (7.1)	12 (27.9)	8 (9.6)	28 (24.6)	15 (23.8)	70 (17.7)
	<i>P. aeruginosa</i>	1 (11.1)	3 (13.0)	3 (16.7)	4 (9.5)	8 (18.6)	11 (13.3)	11 (9.6)	3 (4.8)	44 (11.1)
	<i>Acinetobacter</i> species	0 (0.0)	0 (0.0)	2 (11.1)	7 (16.7)	7 (16.3)	16 (19.3)	9 (7.9)	9 (14.3)	50 (12.6)
	<b>Total</b>	9 (2.3)	23 (5.8)	18 (4.5)	42 (10.6)	43 (10.9)	83 (21.0)	114 (28.9)	63 (16.0)	395 (100.0)
Urine	<i>E. coli</i>	15(83.3)	29(80.6)	29(65.9)	36(72.0)	42(77.8)	31(67.4)	27(64.3)	42(72.4)	251 (72.1)
	<i>Klebsiella</i> species	3(16.7)	4(11.1)	7(15.9)	3(6.0)	4(7.4)	8(17.4)	7(16.7)	10(17.2)	46 (13.2)
	<i>P. aeruginosa</i>	0(0.0)	2(5.5)	3(6.8)	3(6.0)	4(7.4)	5(10.9)	7(16.7)	4(6.9)	28 (8.0)
	<i>Acinetobacter</i> species	0(0.0)	1(2.8)	5(11.4)	8(16.0)	4(7.4)	2(4.3)	1(2.4)	2(3.4)	23 (6.6)
	<b>Total</b>	18(5.2)	36(10.3)	44(12.6)	50(14.4)	54(15.5)	46(13.2)	42(12.1)	58(16.7)	348(100.0)
Blood	<i>E. coli</i>	7(87.5)	7(38.9)	10(43.5)	21(37.5)	21(38.9)	11(39.3)	24(48.0)	19(39.6)	120 (42.1)
	<i>Klebsiella</i> species	1(12.5)	7(38.9)	5(21.7)	5(8.9)	8(14.8)	7(25.0)	17(34.0)	17(35.4)	67 (23.5)
	<i>P. aeruginosa</i>	0(0.0)	3(16.6)	0(0.0)	3(5.4)	3(5.5)	1(3.6)	1(2.0)	4(8.3)	15 (5.3)
	<i>Acinetobacter</i> species	0(0.0)	1(5.5)	8(34.8)	27(48.2)	22(40.7)	9(32.1)	8(16.0)	8(16.7)	83 (29.1)
	<b>Total</b>	8(2.8)	18(6.3)	23(8.1)	56(19.7)	54(19.0)	28(9.8)	50(17.5)	48(16.8)	285(100.0)
Wound	<i>E. coli</i>	4(66.7)	4(66.7)	2(40.0)	8(23.5)	1(20.0)	16(57.1)	16(47.1)	5(33.3)	56 (42.1)
	<i>Klebsiella</i> species	2(33.3)	1(16.7)	3(60.0)	5(14.7)	1(20.0)	4(14.3)	13(38.2)	5(33.3)	34 (25.6)
	<i>P. aeruginosa</i>	0(0.0)	0(0.0)	0(0.0)	10(29.4)	1(20.0)	3(10.7)	4(11.8)	0(0.0)	18 (13.5)
	<i>Acinetobacter</i> species	0(0.0)	1(66.7)	0(0.0)	11(32.4)	2(40.0)	5(17.9)	1(2.9)	5(33.3)	25 (18.8)
	<b>Total</b>	6(4.5)	6(4.5)	5(3.7)	34(25.6)	5(3.7)	28(21.1)	34(25.6)	15(11.3)	133(100.0)
Other	<i>E. coli</i>	7(58.3)	8(50.0)	7(41.2)	12(36.4)	10(38.5)	13(40.6)	9(25.7)	13(36.1)	79 (38.2)
	<i>Klebsiella</i> species	2(16.7)	3(18.75)	2(11.7)	4(12.1)	4(15.4)	6(18.7)	13(37.1)	4(11.1)	38 (18.3)
	<i>P. aeruginosa</i>	3(25.0)	3(18.5)	2(11.7)	4(12.1)	8(30.7)	0(0.0)	9(25.7)	11(30.6)	40 (19.3)
	<i>Acinetobacter</i> species	0(0.0)	2(12.5)	6(35.3)	13(39.4)	1(5.4)	13(40.6)	4(11.4)	8(22.2)	50 (24.1)
	<b>Total</b>	12(5.8)	16(7.7)	17(8.2)	33 (15.9)	26(12.6)	32(15.5)	35(16.9)	36 (17.4)	207(100.0)

\* The majority of respiratory tract samples were sputum, while the minority was respiratory tubes.

# Pus samples were mainly exudates collected from prospective wounds or abscesses.



**Table 3.** Trends of *E. coli* resistance to antibiotics isolated from different clinical samples collected from inpatients admitted to the USTH, Sana'a (2006-2013)

Antibiotic	<i>E. coli</i> resistance to antibiotics per year								P value	Trend
	Number of isolates (resistance %)									
	2006	2007	2008	2009	2010	2011	2012	2013		
Imipenem	23(0.0)	66(1.5)	63(0.0)	101(0.0)	105(3.8)	126(1.6)	155(0.6)	134(9.7)	0.001	↑
Meropenem	--(ND)	8(0.0)	28(0.0)	15(0.0)	--(ND)	--(ND)	29(0.0)	57(14.0)	0.009	↑
Pipracillin-tazobactam	8(0.0)	54(1.9)	60(10.0)	105(1.9)	86(2.3)	121(5.8)	164(9.8)	138(27.5)	<0.001	↑
Cefepime	--(ND)	2(100.0)	17(58.8)	58(32.8)	46(76.1)	123(81.3)	156(70.5)	131(84.0)	<0.001	↑
Ceftazidim	38(44.7)	57(35.1)	63(30.2)	95(35.8)	98(45.9)	120(68.3)	148(64.2)	139(82.7)	<0.001	↑
Ciprofloxacin	35(60.0)	48(52.1)	59(52.5)	66(57.6)	76(75.0)	119(72.3)	152(65.1)	122(82.0)	<0.001	↑
Levofloxacin	--(ND)	25(28.0)	10(40.0)	43(37.2)	81(71.6)	118(49.2)	153(53.6)	92(71.7)	<0.001	↑
Moxifloxacin	--(ND)	--(ND)	8(25.0)	21(33.3)	50(46.0)	112(74.1)	152(69.1)	63(81.0)	<0.001	↑
Amikacin	24(12.5)	45(2.2)	40(10.0)	80(5.0)	77(3.9)	125(0.8)	157(1.9)	133(3.0)	0.014	↓
Gentamicin	25(64.0)	43(39.5)	60(43.3)	30(66.7)	52(48.1)	120(40.0)	156(34.0)	119(41.2)	0.021	↑
Ampicillin-sulbactam	--(ND)	30(83.3)	29(89.7)	65(92.3)	4(75.0)	--(ND)	2(100.0)	34(76.5)	0.171	-
Cefoperazone-sulbactam	--(ND)	15(26.7)	24(0.0)	--(ND)	4(0.0)	122(13.9)	151(9.3)	83(16.9)	0.696	-
Polymyxin	--(ND)	--(ND)	--(ND)	--(ND)	--(ND)	--(ND)	--(ND)	--(ND)	NA	NA

ND, not determined; NA, not applicable.

**Table 4.** Trends of *Acinetobacter* species resistance to antibiotics isolated from different clinical samples collected from inpatients admitted to the USTH, Sana'a (2006-2013)

Antibiotic	<i>Acinetobacter</i> species resistance to antibiotics per year								P value	Trend
	Number of isolates (resistance %)									
	2006	2007	2008	2009	2010	2011	2012	2013		
Imipenem	1(0.0)	6(16.7)	40(52.5)	90(55.6)	75(46.7)	88(80.7)	79(87.3)	97(82.5)	<0.001	↑
Meropenem	--(ND)	4(100.0)	16(50.0)	19(94.7)	--(ND)	--(ND)	14(92.9)	2(100.0)	0.061	-
Pipracillin-tazobactam	1(0.0)	6(0.0)	18(77.8)	100(46.0)	78(11.5)	89(62.9)	77(88.3)	76(86.8)	<0.001	↑
Cefepime	--(ND)	3(100.0)	12(91.7)	53(88.7)	34(85.3)	94(100.0)	75(98.7)	96(99.0)	<0.001	↑
Ceftazidim	1(100.0)	3(66.7)	40(82.5)	88(69.3)	88(83.0)	93(98.9)	80(95.0)	97(99.0)	<0.001	↑
Ciprofloxacin	1(100.0)	6(33.3)	25(64.0)	68(85.3)	71(83.1)	90(96.7)	64(100.0)	83(100.0)	<0.001	↑
Levofloxacin	--(ND)	1(0.0)	7(71.4)	44(56.8)	70(72.9)	92(41.3)	78(60.3)	78(88.5)	0.004	↑
Moxifloxacin	--(ND)	--(ND)	7(57.1)	27(40.7)	41(41.5)	92(79.3)	69(98.6)	34(94.1)	<0.001	↑
Amikacin	--(ND)	1(0.0)	27(59.3)	73(56.2)	71(53.5)	94(75.5)	78(76.9)	71(73.2)	0.001	↑
Gentamicin	1(0.0)	5(80.0)	34(64.7)	30(86.7)	44(90.9)	87(86.2)	76(71.1)	76(75.0)	0.774	-
Ampicillin-sulbactam	--(ND)	4(75.0)	--(ND)	60(76.7)	2(100.0)	--(ND)	2(100.0)	41(95.1)	0.011	↑
Cefoperazone-sulbactam	--(ND)	2(50.0)	18(5.6)	26(7.7)	5(100.0)	90(78.9)	79(78.5)	79(69.6)	<0.001	↑
Polymyxin	--(ND)	--(ND)	7(28.6)	42(14.3)	27(11.1)	93(1.1)	81(0.0)	90(0.0)	<0.001	↓

ND, not determined.



**Table 5.** Trends of *Klebsiella* species resistance to antibiotics isolated from different clinical samples collected from inpatients admitted to the USTH, Sana'a (2006–2013)

Antibiotic	<i>Klebsiella</i> species resistance to antibiotics per year								P value	Trend
	Number of isolates (resistance %)									
	2006	2007	2008	2009	2010	2011	2012	2013		
Imipenem	11(9.1)	28(0.0)	29(10.3)	37(5.4)	55(1.8)	50(4.0)	114(14.9)	74(23.0)	<0.001	↑
Meropenem	--(ND)	5(0.0)	2(0.0)	13(15.4)	--(ND)	--(ND)	28(17.9)	30(33.3)	0.059	-
Pipracillin-tazobactam	4(0.0)	31(0.0)	25(4.0)	36(16.7)	49(2.0)	52(13.5)	113(41.6)	77(49.4)	<0.001	↑
Cefepime	--(ND)	--(ND)	8(75.0)	23(56.5)	34(58.8)	47(70.2)	110(75.5)	77(83.1)	0.004	↑
Ceftazidim	14(64.3)	24(54.2)	29(82.8)	30(73.3)	50(56.0)	50(60.0)	105(79.0)	78(84.6)	0.007	↑
Ciprofloxacin	14(28.6)	18(27.8)	25(44.0)	30(23.3)	41(46.3)	49(46.9)	93(60.2)	66(50.0)	0.001	↑
Levofloxacin	--(ND)	9(22.2)	7(42.9)	11(27.3)	40(37.5)	47(17.0)	98(46.9)	55(50.0)	0.018	↑
Moxifloxacin	--(ND)	--(ND)	8(37.5)	5(40.0)	22(27.3)	46(34.8)	96(68.8)	34(58.8)	0.001	↑
Amikacin	9(0.0)	19(5.3)	18(22.2)	24(12.5)	48(0.0)	50(8.0)	110(10.9)	74(16.2)	0.151	-
Gentamicin	16(56.3)	24(70.8)	22(68.2)	7(100.0)	38(42.1)	43(55.8)	103(49.5)	66(53.0)	0.062	-
Ampicillin-sulbactam	--(ND)	11(90.9)	11(100.0)	20(90.0)	--(ND)	--(ND)	1(100.0)	29(86.2)	0.359	-
Cefoperazone-sulbactam	--(ND)	11(9.1)	18(5.6)	6(16.7)	1(0.0)	47(14.9)	103(46.6)	49(53.1)	<0.001	↑
Polymyxin	--(ND)	--(ND)	--(ND)	--(ND)	--(ND)	--(ND)	--(ND)	--(ND)	NA	NA

ND, not determined; NA, not applicable.

**Table 6.** Trends of *P. aeruginosa* resistance to antibiotics isolated from different clinical samples collected from inpatients admitted to the USTH, Sana'a (2006–2013)

Antibiotic	<i>P. aeruginosa</i> resistance to antibiotics per year								P value	Trend
	Number of isolates (resistance %)									
	2006	2007	2008	2009	2010	2011	2012	2013		
Imipenem	4(0.0)	18(11.1)	11(36.4)	14(42.9)	38(7.9)	33(15.2)	40(15.0)	28(39.3)	0.296	-
Meropenem	--(ND)	3(0.0)	6(16.7)	5(40.0)	--(ND)	--(ND)	6(33.3)	13(30.8)	0.391	-
Pipracillin-tazobactam	3(0.0)	19(0.0)	13(23.1)	30(16.7)	37(10.8)	32(6.3)	39(15.4)	29(20.7)	0.194	-
Cefepime	--(ND)	1(0.0)	3(66.7)	15(33.3)	20(40.0)	32(40.6)	38(34.2)	31(32.3)	0.576	-
Ceftazidim	4(25.0)	17(23.5)	10(50.0)	28(32.1)	35(31.4)	34(26.5)	19(36.8)	30(53.3)	0.110	-
Ciprofloxacin	5(60.0)	14(28.6)	13(46.2)	24(25.0)	25(40.0)	31(16.1)	37(21.6)	24(41.7)	0.370	-
Levofloxacin	--(ND)	8(37.5)	1(0.0)	20(30.0)	18(33.3)	31(19.4)	36(19.4)	17(47.1)	0.934	-
Moxifloxacin	--(ND)	--(ND)	2(50.0)	9(22.2)	13(46.2)	31(19.4)	36(47.2)	11(54.5)	0.159	-
Amikacin	2(50.0)	14(0.0)	8(37.5)	19(5.3)	36(5.6)	34(11.8)	39(10.3)	28(35.7)	0.063	-
Gentamicin	5(60.0)	13(30.8)	9(77.8)	13(46.2)	24(33.3)	33(18.2)	39(17.9)	27(25.9)	0.004	↓
Ampicillin-sulbactam	--(ND)	--(ND)	--(ND)	--(ND)	--(ND)	--(ND)	--(ND)	--(ND)	NA	NA
Cefoperazone-sulbactam	--(ND)	--(ND)	--(ND)	--(ND)	--(ND)	--(ND)	--(ND)	--(ND)	NA	NA
Polymyxin	--(ND)	--(ND)	--(ND)	--(ND)	--(ND)	--(ND)	--(ND)	--(ND)	NA	NA

ND, not determined; NA, not applicable.



The most frequently isolated species from the inpatients admitted to the departments of the USTH were *E. coli* (41.6%) and *Acinetobacter* species (26.7%) followed by *Klebsiella* species (21.0%) and *P. aeruginosa* (10.6%). In line with these findings, *E. coli* was the most frequently isolated species in Iran (71.9%), Saudi Arabia (38.3%) and Rwanda (35.7%). Nonetheless, *Klebsiella* species was the second most frequently isolated bacteria in the above-mentioned countries (1, 22, 23).

The present study showed an emerging crisis of antibiotic resistance among the most isolated Gram-negative bacteria, where the highest rate of resistance was observed for *Acinetobacter* species that presented a dramatically rising trend of resistance to most antibiotics. Only polymyxin remains active against *Acinetobacter* species. This finding is consistent with that reported from China, where the susceptibility of *Acinetobacter baumannii* to most antibiotics, including cephalosporins, quinolones, aminoglycosides and carbapenems, decreased over a four-year period (24). However, polymyxin was not tested in the latter study.

Resistance of *E. coli* and *Klebsiella* species to fluoroquinolones, piperacillin-tazobactam, ceftazidime and cefepime increased significantly over the years, while only amikacin was activity against these two species. This finding is similar to that reported from Rwanda, where *E. coli* and *Klebsiella* species had a high resistance rate to penicillins, quinolones and the third-generation cephalosporins (23). In contrast to the findings of the present study, gentamicin and ciprofloxacin still showed a reasonable activity against *E. coli* in northern Ethiopia (25).

In the present study, the unchanging resistance rate of *P. aeruginosa* to most antibiotics could be contributed to the small number of isolates in the USTH over the years of the study. However, *P. aeruginosa* is one of the most antibi-

otic-resistant bacteria worldwide, contributing to ICU-acquired infections with limited empirical therapy options (26, 27). In contrast, the susceptibility of *P. aeruginosa* to gentamicin, ceftazidime and ciprofloxacin decreased significantly in Saudi Arabia, while the trend of resistance to carbapenems, amikacin and piperacillin-tazobactam was not dramatically changed over a 7-year period (1998-2004) (28). In the United States, the National Nosocomial Infection Surveillance (NNIS) survey data of the Centers for Disease Prevention and Control found a dramatic decrease in the susceptibility rate of *P. aeruginosa* to both imipenem and quinolones (29).

The present study demonstrated that Gram-negative bacterial isolates have high incidence of resistance to commonly used antibiotics among inpatients admitted to the USTH. All bacterial isolates showed an elevated rate of resistance to third- and fourth-generation cephalosporins and quinolones. Several factors could contribute to such an increased rate of resistance including misuse of antibiotics by healthcare providers, lack of surveillance data that would be helpful for choosing proper empirical therapy and use of broad-spectrum antibiotics for a long duration (more than 7 days).

Although this study provides data on antibiotic resistance over an eight-year period from one of the leading healthcare hospitals in Sana'a, it has a number of limitations. First, not all antibiotics were tested with the same frequency of isolates. Second, antibiotic susceptibility was tested for all inpatients, including those in ICU. This, in turn, may lead to an over estimation of the antibiotic resistance rate because most ICU patients usually have more virulent bacterial infections than those in other inpatient departments as a result of co-morbidities, more frequent use of mechanical ventilation and intravascular devices. Furthermore, due to the limited availability of resources at the time of the study,



only data in the period from 2006 to 2013 were analyzed.

## 5. Conclusions

Antibiotic resistance is a recognizable problem among inpatients admitted to different departments of tertiary care hospitals and centers. Of the most frequently isolated Gram-negative bacteria, *Acinetobacter* species has the highest resistance rate to the most commonly used antibiotics, where only polymyxin B is effective against this species. *P. aeruginosa* shows an unchanging rate of resistance to antibiotics in the USTH despite being quite resistant to antibiotics on a global scale, which could be attributed to the smaller number of *P. aeruginosa* isolates tested over the study period. Further large-scale studies on the trends of antibiotic resistance rates in hospital-based settings and the best ways to counteract such resistance in Yemen are recommended.

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## Authors' contributions

MK, AZ, DA and MA contributed to the study design, analysis and manuscript writing. MK and MA drafted and revised the manuscript. All authors approved the final version.

## Competing interests

The authors declare that they have no competing interests associated with this article.

## Ethical approval

Ethical approval was obtained from the Ethics Committee of the USTH, UST, Sana'a, Yemen.

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