

# Trends in the Annual Incidence of Carbapenem Resistant among Gram Negative Bacilli in a Large Teaching Hospital in Makkah City, Saudi Arabia

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## Abstract

**Objective:** To detect the prevalence of carbapenem resistance among Gram negative bacilli at the Al-Noor Specialist Hospital in the western part of Saudi Arabia. **Materials and Methods:** This study was conducted in the Microbiology department, Al-Noor Specialist Hospital, Makkah city, Saudi Arabia. The clinical samples were collected from admitted patients in the wards, Intensive Care Units (ICUs), urology unit and surgery unit, these samples included blood, urine, sputum, pus and wound. The identification and antibiotic susceptibility testing of all bacterial isolates were performed via the Vitek 2 Compact System. **Results:** Out of 4803 Gram negative bacterial bacilli were isolated, the prevalence rate of carbapenem resistance among these isolates was 2797/4803 (58.23%), and sensitivity rate was 2006/4803 (41.77%) of the total isolates. The rate of resistance to carbapenem was among *Acinetobacter baumannii* 1710 (99.13%), followed by *Pseudomonas aeruginosa* 575 (62.4%), *Klebsiella pneumoniae* 459 (38%) and *Escherichia coli* 56 (5.59%). The trend of carbapenem resistance among Gram negative bacterial isolates from 2013-2015 was 53.99%, 59.88% and 61.43% respectively. **Conclusion:** *A. baumannii* recorded, the highest rate of carbapenem resistance through three year, 98.19%, 99.48% and 99.81% respectively and the lowest rate of resistance recorded with *E. coli*, 4.63%, 5.79% and 6.31% respectively.

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## Keywords

Carbapenem Resistance, *Acinetobacter baumannii*, Makah, Pathogens

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## 1. Introduction

Carbapenems antibiotics, which include imipenem, meropenem, doripenem and ertapenem, have very significant role for treating severe bacterial infections. They quickly enter to the cell wall through the proteins found in the outer membrane (PBPs) in Gram negative bacteria [1] [2]. This group of antibiotics are the most common used in treatment of infections that life threatening, as well as they used as last line for treating and defense against multidrug resistant strains such as *Acinetobacter baumannii*, *Pseudomonas aeruginosa*, *Klebsiella pneumoniae* and *Escherichia coli* [3] [4]. These bacteria species are the most common pathogens of human and considered as main cause of hospital acquired infections. Nosocomial infections have a significant role in transmission of resistant strains [5]. In recent years, there is a quick decline in the effectiveness of carbapenems antibiotics in treatment of serious bacterial infections, which considered a threat to public health [6] [7] [8]. Carbapenems resistance may occur, due to the secretion of enzymes and genes which are responsible from reduced susceptibility and resistance to carbapenems such as oxacillinase-48 (OXA-48), *Klebsiella pneumoniae* carbapenemase (KPC) and New Delhi metallo-beta-lactamase-1 (NDM-1). Horizontal gene transfer mechanisms like transformation, transduction and conjugation can spread resistance genes, as well and these enzymes have the ability to break down carbapenems and prevent them from reaching PBPs, makes them ineffective [9] [10] [11]. World Health Organization (WHO) reported that infections caused by Gram negative bacterial bacilli threaten the lives of many patients in intensive care units (ICUs) around the world due to its resistance to carbapenems, and the rate of mortality among those patients ranges from 25% to 75% [12]. The studies have indicated that carbapenems resistance among Gram negative bacteria has become a global issue [13]. Recent studies showed that Saudi Arabia is considered among the countries that reported high rates of antimicrobial resistance [14] [15]. Thus, this study aimed to detect the prevalence of carbapenem resistance among Gram negative bacteria at the Al-Noor Specialist Hospital in the western part of Saudi Arabia, and monitoring to carbapenem resistance among these types of bacteria in order to devise strategies to counter threats from these extremely dangerous bacteria.

## 2. Materials and Methods

Specimens collection and processing, this study was conducted at the microbiology department in the Al-Noor Specialist Hospital, Makah city, Saudi Arabia, during three years from November 2012 to December 2015. Clinical specimens were collected from patients in three wards in the hospital, Intensive Care Unit

(ICU), Urology and Surgery units, these samples included blood, urine, sputum, pus and wound swabs.

Bacterial isolation and identification, all clinical specimens were cultured on blood agar, MacConkey's agar and incubated under aerobic conditions for 24 hours at 37°C. The identification of isolated organisms was carried out by colonial morphology, Gram stained films and the species identification performed via the VITEK 2 Compact System (Bio-Merieux).

Antibiotic susceptibility testing, for isolated organisms such as *Acinetobacter baumannii*, *Pseudomonas aeruginosa*, *Klebsiella pneumonia* and *Escherichia coli* were carried out by VITEK 2 Compact System (Bio-Merieux). The isolates which were showed elevated MIC to meropenem and imipenem; as well as resistance to ceftriaxone, cefotaxime and ceftazidime (Third generation cephalosporin's) were considered to be carbapenem resistant. The resistance breakpoints used for detecting carbapenem resistance was  $\geq 4$  µg/ml for imipenem and meropenem. The resistance breakpoints used for ceftazidime and cefotaxime were  $\geq 32$  µg/ml where ceftriaxone was  $\geq 64$  µg/ml, according to Clinical and Laboratory Standards Institute (CLSI) guidelines.

### 3. Results

Out of 4803 Gram negative bacilli isolated from different clinical specimens in this study, The prevalence rate of carbapenem resistance among Gram-negative isolates were 2797/4803 (58.23%), and sensitivity rate were 2006/4803 (41.77%) of the total isolates, 1001 (20.84%) was *E. coli*, 1158 (24.10%) *K. pneumonia*, 922 (19.19%) *P. aeruginosa* and 1722 (35.85%) *A. baumannii*. The maximum number of isolated bacteria was from sputum 1773 (36.91), followed by wound swabs 1513 (31.50%), blood 913 (19%), urine 566 (11.78%) and Pus 38 (0.79%). The high rate of resistance between both meropenem and imipenem was *A. baumannii* 1710/1722 (99.13%), followed by *p. aeruginosa* 575/922 (62.4%), *K. pneumoniae* 459/1158 (38%) and *E. coli* 56/1001 (5.59%) (Table 1).

Majority of resistant strains among different locations of the hospital, were isolated from ICU, 3573/4803 (74.39%), followed by 1044/4803 (21.73%) from surgery unit and 186/4803 (3.87) from urology unit.

*A. baumannii* was the most common microorganism isolated from ICU patients (Table 2).

The trend of carbapenem resistance among Gram-negative bacterial isolates from November 2012 to December 2015 was 933/1728 (53.99%), 972/1623 (59.88%) and 892/1452 (61.43%) respectively. In 2013, 1728 isolates were examined for Carbapenem resistance, among of these isolates, 933 (53.99%) strains were resistant to carbapenem included *A. baumannii* 98.19% (597/608), *P. aeruginosa* 53.63% (192/358), *K. pneumonia* 30.69% (128/417) and *E. coil* 4.63% (16/345). In 2014, 1623 isolates were examined for Carbapenem resistance, among of these isolates, 972 (59.88%) strains were resistant to carbapenems, included *A. baumannii* 99.48% (581/584), *P. aeruginosa* 58.30% (207/355), *K. pneumonia*

**Table 1.** Rate of carbapenems resistance among Gram negative bacterial isolates in clinical samples.

Frequency (n) & %	Gram Negative Bacterial Isolates											
	<i>E. coli</i>			<i>K. pneumonia</i>			<i>P. aeruginosa</i>			<i>A. baumannii</i>		
	Carbapenem sensitive n (%)	Carbapenem resistant n (%)	Total n	Carbapenem sensitive n (%)	Carbapenem resistant n (%)	Total n	Carbapenem sensitive n (%)	Carbapenem resistant n (%)	Total n	Carbapenem sensitive n (%)	Carbapenem resistant n (%)	Total n
URINE 566 (11.78%)	309 (97.2%)	9 (3.8%)	318	112 (72%)	44 (28%)	156	24 (50%)	24 (51%)	48	0 (0%)	44 (100%)	44
Sputum 1773 (36.91)	91 (82%)	20 (12%)	111	126 (43%)	166 (47%)	292	122 (31%)	273 (69%)	395	4 (0.4%)	971 (99.6%)	975
Blood 913 (19%)	258 (95%)	14 (5%)	272	234 (64%)	132 (36%)	366	25 (54%)	24 (46%)	46	4 (1.7%)	225 (98.3%)	229
Pus 38 (0.79%)	19 (93%)	2 (7%)	21	8 (64%)	4 (36%)	12	0 (0%)	3 (100%)	3	0 (0%)	2 (100%)	2
Wound 1513 (31.50%)	268 (96%)	11 (4%)	279	219 (66%)	113 (34%)	332	232 (54%)	198 (46%)	430	7 (1.5%)	465 (98.5%)	472
Total 4803	945 (92.6%)	56 (5.59%)	1001	699 (62%)	459 (38%)	1158	347 (37.6%)	575 (62.4%)	922	12 (0.7%)	1710 (99.3%)	1722

**Table 2.** Distribution of carbapenems resistant strains among different locations.

Locations	Carbapenems resistant strains %				
	<i>E. coli</i> n (%)	<i>K. pneumonia</i> n (%)	<i>P. aeruginosa</i> n (%)	<i>A. baumannii</i> n (%)	Total n (%)
ICU	549 (15.36)	888 (24.85)	628 (17.57)	1508 (42.20)	3573 (74.40%)
Surgery	361 (34.57)	225 (21.55)	273 (26.14)	185 (17.72)	1044 (21.73%)
UROLOGY	91 (48.92)	45 (24.19)	21 (11.29)	29 (15.59)	186 (3.87%)
Total	1001 (20.85)	1158 (24.10)	922 (19.20)	1722 (35.85)	4803 (100%)

41.17% (168/408) and *E. coli* 5.79% (16/276). In 2015, 1452 isolates were examined for Carbapenem resistance as well, among these isolates, 892 (61.43%) strains were resistant to carbapenems, included *A. baumannii* 99.81% (529/530),

*P. aeruginosa* 84.21% (176/209), *K. pneumonia* 54.27% (163/333) and *E. coli* 6.31% (24/380). Organisms showed increasing trend of carbapenem resistance among Gram-negative bacterial isolates from 2013-2015, generally the highest rate of carbapenem resistance during the three years was *A. baumannii* which recorded 98.19%, 99.48% and 99.81% respectively and the lowest rate of carbapenem resistance was *E. coli* which recorded 4.63%, 5.79% and 6.31% respectively (Table 3).

#### 4. Discussion

In recent years, carbapenem resistance in Gram negative bacteria has been reported worldwide with increasing frequency. Carbapenemase production is a mechanism of carbapenem resistance. Carbapenem hydrolyzing enzymes are most commonly seen in *P. aeruginosa* and *A. baumannii*, however in the recent years, there are an increasing incidence of these enzymes in *K. pneumoniae* and *E. coli*. In the current study, 2797 (58.23%) of the total 4803 Gram negative bacterial isolates were resistant to carbapenems, *A. baumannii* was the most common isolates among this group followed by *P. aeruginosa*, *K. pneumonia* and *E. coli* respectively. This study shown a high rate of carbapenem resistant among Gram negative bacterial isolates at Al-Noor Specialist Hospital compared to previous studies from Saudi Arabia. Recent studies from Egypt showed that, carbapenem resistance among *A. baumannii* strains recorded (74%) [16]. Some studies from Jordan reported a high rate of resistance to meropenem and imipenem; (70.1% and 71.6% respectively) among *A. baumannii* in clinical isolates [17]. Where *A. baumannii*, *P. aeruginosa* were recorded resistance to carbapenem in this study 99.81%, 84.21% respectively. Recent study in Saudi Arabia showed that an increase in imipenem resistance among *P. aeruginosa* isolates increased from 20% in 2004 to 38.57% in 2011, another study in 2009 and 2010 reported the

**Table 3.** Organisms showing trend of carbapenem resistance among Gram-negative bacterial isolates from 2013-2015.

year	Resistance rate per year								Total of carbapenem resistant organisms
	<i>E. coli</i>		<i>K. pneumonia</i>		<i>P. aeruginosa</i>		<i>A. baumannii</i>		
	Total No.	Carbapenem Resistant n (%)	Total No.	Carbapenem Resistant n (%)	Total No.	Carbapenem Resistant n (%)	Total No.	Carbapenem Resistant n (%)	
2013	345	16 4.63%	417	128 30.69%	358	192 53.63%	608	597 98.19%	933/1728 (53.99%)
2014	276	16 5.79%	408	168 41.17%	355	207 58.30%	584	581 99.48%	972/1623 (59.88%)
2015	380	24 6.31%	333	163 54.27%	209	176 84.21%	530	529 99.81%	892/1452 (61.43%)
Total	1001	56 (5.59%)	1158	459 (39.63%)	922	575 (62.36%)	1722	1707 (99.12%)	2797/4803

high rate of carbapenem resistance among *P. aeruginosa* isolates ranged from 36% to 53% to meropenem and imipenem respectively [18] [19]. Several studies around the world shown increasing trend of carbapenem resistant among *P. aeruginosa* ranged from (4% - 60%), thus, *P. aeruginosa* and *A. baumannii* became constituted risks according to many reports [20] [21]. This study shown that, carbapenem resistance among *K. pneumonia* isolates were 30.69%, 41.17% and 54.27% respectively, followed by *E. coli* which was 4.63%, 5.79% and 6.31% respectively during the three years. The degree of carbapenem resistance in the current study was higher than the results in a study conducted in Egypt in 2013 concluded that carbapenem resistance enterobacteriaceae were, 53% to meropenem and 36% to imipenem [22]. In Saudi Arabia, a study reported high rate of carbapenem resistance 48% among *K. pneumonia* isolates, as well as another studies from Gulf countries confirmed emergence of NDM-1 and OXA-48 among *K. pneumonia* strains in Saudi Arabia, Kuwait, Oman and United Arab Emirates [23] [24] [25].

## 5. Conclusion

The current study reported increasing to carbapenem resistance among Gram negative isolates. The highest rate of carbapenem resistance in this study was observed among *A. baumannii* and *P. aeruginosa* respectively. *A. baumannii* was the most common microorganism isolated from ICU patients. The high rates of carbapenem resistance among Gram negative isolates are worrisome and require steric application of surveillance systems and infection control as well as early detection and the accurate selection of antibiotics in clinical practice against these microorganisms. However, this study highlighted the current situation of carbapenem resistance amongst Gram negative bacterial isolates in this region.

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## Conflict of Interest

The authors declare no conflict of interest.

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