

# Incidence of infection by carbapenem-resistant Enterobacteriaceae in patients with positive surveillance culture in the intensive care unit

Pablo Villa<sup>1</sup>, Alicia Hidrón<sup>1,2,3</sup>, Carlos Restrepo<sup>4</sup>, Natalia Zapata<sup>2</sup>, Viviana Gómez<sup>2</sup>, Mónica Zuluaga<sup>2</sup>, Sara Penagos<sup>5</sup>, Faíver Ramírez<sup>4,5</sup>, Patricia Sierra<sup>4</sup>, Andrés Colina<sup>1</sup>, Manuela Vélez<sup>1</sup>, Camila Cruz<sup>1</sup>, Esteban Vallejo<sup>1</sup>, Ana Valencia<sup>1</sup>, Carlos Agudelo<sup>1,5,6</sup>

<sup>1</sup> Escuela de ciencias de la salud, Universidad Pontificia Bolivariana, Medellín, Colombia, <sup>2</sup> Hospital PabloTobón Uribe, Medellín, Colombia <sup>3</sup> Emory University School of Medicine, Atlanta, GA, USA  
<sup>4</sup> IPS Universitaria Clínica León XIII, Medellín, Colombia, <sup>5</sup> Centros Especializados de San Vicente Fundación, Medellín, Colombia, <sup>6</sup> Clínica Universitaria Bolivariana, Medellín, Colombia

## Abstract

**Introduction:** Some intensive care units (ICU) perform an active search of carbapenem resistant Enterobacteriaceae (CRE) with epidemiological surveillance cultures. Nonetheless, the incidence of infection by these colonizing microorganisms is not clear yet. The main objective was to describe the incidence of infection by CRE, phenotypically identic to the colonizing microorganism.

**Material/methods:** From January 1, 2014 through December 31, 2015, we conducted a retrospective cohort study in three ICUs in Medellín, Colombia. Patients with a positive surveillance culture for CRE during ICU hospitalization where included.

**Results:** A total of 177 patients had a positive epidemiological surveillance culture for CRE. The majority of patients were men (62,1%), with a median age of 64 years (RIQ 25). The most frequently isolated microorganism were *Klebsiella pneumoniae* 143 (80,7%), and the most important comorbidity was diabetes mellitus 51 (28,8%).

29,9% (53) of colonized patients got infected; of these, 39 patients (73,5%) got infected by a gram negative rod (GNR) different to the colonizing strain and 14 patients (26,4%) got infected by the same colonizing CRE. The global incidence of infection by CRE was 7,9% and the density of incidence of infection was 3,1/1000 days of ICU admission. Of the 14 patients infected by CRE, 11 patients (78,5%) died vs. 19 (48,7%) of patients infected by GNR different from the colonizing strain and 36 (29%) of colonized patients that did not get infected. In the multivariate analysis, the only independent predictor of infection by the same colonizing CRE was solid organ cancer (RR 7,3; 95% CI 1,52-35,6).

**Conclusions:** In this cohort of critically ill patients colonized by CRE, the infection rate was higher than expected, with solid organ cancer being a predictor of infection.

## Introduction

Since the first report of *Klebsiella pneumoniae* resistant to carbapenems in North Carolina in 1996, the number of carbapenem resistant Enterobacteriaceae (CRE) isolates has increased significantly. Endemic levels have been reached in some countries, which has led to declaring it as a public health emergency by the Centers for Disease Control and Prevention (CDC). For this reason some intensive care units (ICU) perform an active search for CRE with epidemiological surveillance cultures. Nonetheless, the incidence of infection by these colonizing microorganisms is not known nor is there clarity on whether it is necessary to initiate empirical therapies directed to CRE in case of active infection. The main objective was to describe the incidence of infection by CRE, phenotypically identic to the colonizing microorganism.

## Methods

From January 1, 2014 through December 31, 2015, we conducted a retrospective cohort study in three ICUs in Medellín, Colombia. Patients >18 years old with a positive surveillance culture for CRE during ICU hospitalization where included. Patients were excluded if they were pregnant, had active CRE infection or prior CRE colonization. A descriptive analysis was performed. Demographic, laboratory and clinical information was collected. Variables with biological plausibility and those with a p value less than 0.05 on bivariate analyses were used in a logistic regression model to identify independent factors associated with infection. All analyses were performed using IBM software SPSS v 17.0.

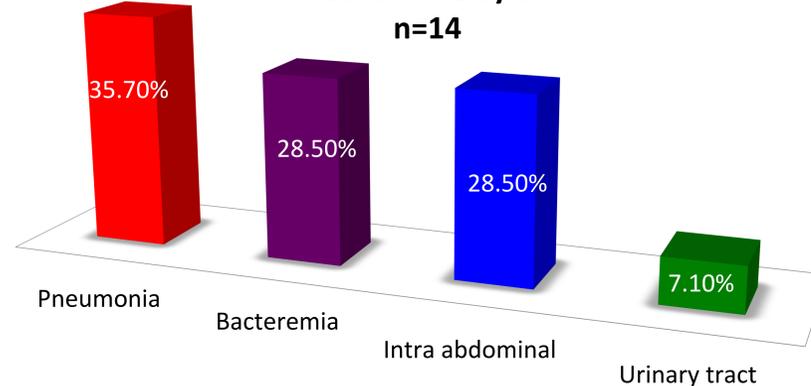
## Results

A total of 177 patients had a positive epidemiological surveillance culture for CRE. 53 (29,9%) of colonized patients got infected; of these, 39 patients (73,5%) got infected by a gram negative rod (GNR) different to the colonizing strain and 14 patients (26,4%) got infected by the same colonizing CRE.

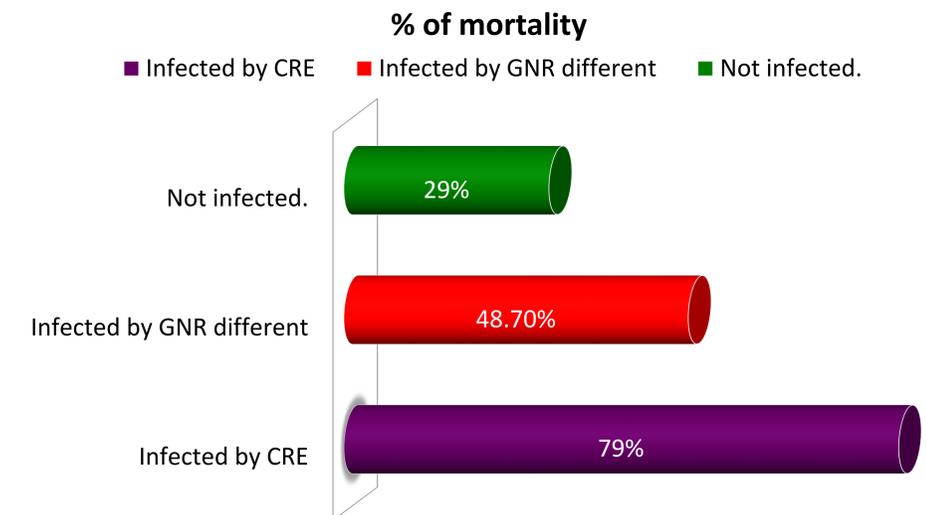
### Characteristics of patients with positive epidemiological surveillance cultures

Characteristics	n= 177
Age (years) Median (IQR)	64 (25)
Male n (%)	110 (62,1)
Microorganism	
<i>Klebsiella pneumoniae</i> (%)	143 (80,8)
<i>Enterobacter cloacae</i> (%)	18 (10,2)
<i>Escherichia coli</i> (%)	10 (5,6)
Others (%)	6 (3,3)
Chronic kidney disease (%)	46 ( 26,0)
Dialysis previous ICU (%)	18 (10,2)
Diabetes Mellitus (%)	51 (28,8)
Coronary heart disease (%)	25 (15,3)
Solid organ cancer (%)	17 (9,6)
Charlson comorbidity index median (IQR)	2 (3,0)
APACHE II score (median) (IQR)	19 (8,0)
Antibiotic previous ICU (%)	134 (75,7)
Dialysis during ICU (%)	66 (37,3)
Central venous catheter (%)	141 (79,0)
Peripherally inserted central venous catheter (%)	12 (6,8)
Nasogastric tube (%)	123 (69)
Invasive ventilation (%)	150 (84,7)
Tracheostomy (%)	48 (27,1)
Endoscopic gastrostomy (%)	5 (2,8)
Surgery during ICU (%)	50 (28,2)

### Infection site by CRE



The global incidence of infection by CRE was 7,9% and the density of incidence of infection was 3,1/1000 days of ICU admission.



## Bivariate analysis

### Bivariate analysis of characteristics associated with infection by CRE

Variable	Infection by CRE (n= 14)	Infection by no CRE (n=163)	p
>65 years old	11 (78,5)	77 (47,2)	0.02
APACHE II score >20	10 ( 71,4)	70 (42,9)	0.03
Solid organ cancer	5 (37,1)	12 (7,36)	< 0,01
Dialysis	9 (64,29)	70 (42,9)	0,01
Peripherally inserted central venous catheter	2 (21,4)	9 (5,5)	0,05
Tracheostomy requirement	7 (50)	41 (25,1)	0.05
Endoscopic procedures	3 (21,4)	8 ( 4,9)	<0,01
Total parenteral nutrition	4 (28,5)	14 (8,58)	0,03

In the multivariate analysis, controlling for age, gender and APACHE-II score at ICU admission, independent predictor of infection by the same colonizing CRE was solid organ cancer (RR 7,3; 95% CI 1,52-35,6).

## Conclusions

In this cohort of critically ill patients colonized by CRE, the infection rate and mortality was higher than expected, with solid organ cancer being a predictor of infection.