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Short report

Evolving epidemiology of carbapenemase-producing Enterobacteriaceae in Portugal: 2012 retrospective cohort at a tertiary hospital in Lisbon

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SUMMARY

Despite great efforts to enhance European epidemiological surveillance on carbapenemase-producing Enterobacteriaceae (CPE), information from several countries remains scarce. To address CPE epidemiology in Portugal, we have undertaken a retrospective cohort study of adults with CPE cultures identified in the microbiology laboratory of a tertiary hospital, in 2012. Sixty patients from 25 wards or intensive care units were identified. This is, to the best of our knowledge, the first report of clinical data on CPE in Portugal. It shows a hospital-wide CPE dissemination and alerts us to an evolving epidemiological situation not previously described.

Introduction

Carbapenemase-producing Enterobacteriaceae (CPE) infections constitute an emerging health threat. *Klebsiella pneumoniae* is of particular concern, given its ability to cause hospital-wide outbreaks.[1] In 2013, according to the European Centre for Disease Prevention and Control, 8.3% of *K. pneumoniae* causing invasive infections in Europe were resistant to carbapenems. A wide range was reported, from 0% in some northern European countries to 59% in Greece.[2] Although great efforts have been made to enhance epidemiological surveillance in Europe, the information from several countries remains scarce.[3]

This article aims to address the epidemiology of CPE in Portugal by characterizing, to the best of our knowledge, the

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first clinical data of patients with CPE isolates from a Portuguese hospital.

Methods

We have conducted a retrospective cohort study of all adult patients with CPE culture identified in the microbiology laboratory from January to December 2012 at Centro Hospitalar de Lisboa Norte (CHLN). CHLN is a university hospital centre located in Lisbon and providing care to a population of 370,000 people. It is composed of two hospitals (with 800 and 300 beds), including 33 specialties. Bacterial identification and antimicrobial susceptibility testing were performed at the microbiology laboratory by automated systems [MicroScan®, Snap-on, Kenosha, WI, USA; or Vitek2®, bioMérieux, Marcy l'Etoile, France; and matrix-assisted laser desorption ionization time-of-flight (MALDI-TOF)] and confirmed by disc diffusion test. Minimum inhibitory concentrations (MICs) of carbapenems were determined by using the agar gradient test (E-test®, AB Biodisk, Solna, Sweden) method following the European Committee on Antimicrobial Susceptibility Testing (EUCAST) guidelines.[4] Isolates with reduced susceptibility to carbapenems were selected for phenotypic confirmation of carbapenemase production through the modified Hodge test.[4] No further analysis was performed in the isolates recovered in the study period. No routine screening for asymptomatic CPE carriage was made. Ethical approval was obtained from the CHLN Ethics Committee for Health. Epidemiological data were collected from clinical records. For data analysis Stata® 13 statistical software (StataCorp., College Station, TX, USA) was used.

Results

Sixty patients with CPE isolates were identified in 25 wards and intensive care units (ICUs). The most relevant clinical data are presented in Table I. Ten patients (17%) were considered to be colonized with CPE according to the clinical care physicians judgement. Bloodstream infections accounted for 22% ($N = 13$) of cases. All patients were hospitalized at the time of CPE isolation, with the exception of two cases identified during outpatient visits after a recent stay in surgical wards (CPE isolated from surgical wound exudates). All patients transferred from other hospitals came from national centres ($N = 13$, 22%). The majority of patients ($N = 39$, 65%), including all six patients with CPE identified in the first 48 h after admission, had been hospitalized in our hospital centre within the last 12 months. The great majority of cases were identified at the 800-bed hospital ($N = 57$, 95%). The department with most cases was haematology (ward and bone marrow transplant unit) (22%, $N = 13$). Case clusters, defined as more than one case diagnosed in the same ward or ICU within the same time-period of in-ward stay, were detected in five wards. More than a third of patients (38%, $N = 23$) had previous antimicrobial therapy with four or more antibiotics administered in the last three months, and the median length of antibiotic therapy before CPE isolation was 24 days (interquartile range: 10–43). The overall in-hospital mortality (all causes) rate was 32% ($N = 19$), but this rate increased to 62% ($N = 8$) when focusing on patients with bloodstream infections.

Klebsiella pneumoniae was the Enterobacteriaceae species most frequently detected (83%, $N = 50$). Overall, 5.3% of all *K. pneumoniae* and 7.8% of *K. pneumoniae* isolated in blood in 2012 at our hospital were carbapenemase producers. Other Enterobacteriaceae species identified were *Klebsiella oxytoca* ($N = 3$), *Enterobacter aerogenes* ($N = 4$), and *Enterobacter*

Table I
Characteristics of patients with carbapenemase-producing Enterobacteriaceae (CPE)

Variable	Patients with CPE
No.	60
Male sex	28 (47%)
Age (years), mean (±SD)	65 (±18)
Anatomical site of isolation	
Urine	23 (38%)
Blood	13 (22%)
Surgical wound exudate	10 (17%)
Pressure ulcer exudate	1 (2%)
Peri-CVC exudate	1 (2%)
Respiratory secretions	8 (13%)
Vascular prosthetic material	2 (3%)
Bile	1 (2%)
External ear exudate	1 (2%)
Origin at hospital admission	
Home	41 (68%)
Transferred from other national hospital	13 (22%)
Long-term care facility	4 (7%)
Outpatient	2 (3%)
Hospital stay in previous year	39 (65%)
Ward at the time of CPE isolation	
Medical wards[a]	29 (48%)
Surgical wards[b]	8 (13%)
Medical or polyvalent ICUs[c]	8 (13%)
Surgical ICUs[d]	13 (22%)
CPE isolation in the first 48 h of hospitalization	6 (10%)
LOS before CPE isolation, median days (IQR)	37 (14–42)
LOS until death or discharge, median days (IQR)	60 (28–67)
Invasive procedures performed before CPE isolation	
CVC	36 (60%)
Surgery	30 (50%)
Mechanical ventilation	26 (43%)
Underlying conditions	
Haematological malignancy	20 (33%)
Chemotherapy	16 (27%)
Neutropenia	11 (18%)
Solid malignancy	11 (18%)
Antibiotic therapy within the last 90 days before CPE isolation	53 (88%)
Piperacillin–tazobactam	32 (53%)
Carbepenems	31 (52%)
Third-generation cephalosporin	12 (20%)
Quinolones	7 (12%)
All-cause in-hospital mortality	19 (32%)

CVC, central venous catheter; ICU, intensive care unit; LOS, length of hospital stay; IQR, interquartile range; SD, standard deviation. Values are no. (%) or as otherwise indicated.

[a] Gastroenterology, haematology, infectious diseases, internal medicine (seven wards), nephrology, neurology, pneumology.

[b] General surgery, orthopaedics, vascular surgery.

[c] General, infectious diseases, marrow transplant unit.

[d] Burn unit, cardiothoracic surgery, general surgery (two ICUs), neurosurgery, orthopaedics.