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Epidemiology of *Klebsiella pneumoniae* MDR during the years 2015-2017 in "G. Martino" University Hospital of Messina: preliminary data

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ABSTRACT

— ***Objective:*** *Klebsiella pneumoniae* is responsible for infections of hospitalized patients and compromised individuals. Persistent exposure of K. pneumoniae to antimicrobial agents facilitated the emergence of multidrug-resistant strains and the non-susceptible. The primary aim of this study was to evaluate the epidemiology of *K. pneumoniae* MDR during the years 2015-2017 in "G. Martino" University Hospital of Messina.

— ***Materials and Methods:*** Vitek 2 automated system (bioMérieux, Italy) was used for isolate identification and antimicrobial susceptibility testing. We focused our attention on the isolates possibly producing carbapenemases.

— ***Results:*** During the period 2015-2017, 1,563 non-duplicated strains of *K. pneumoniae* were isolated from different in patients, specimen and wards in our hospital. We observed a decrease in the occurrence of isolated of the *K. pneumoniae* from blood cultures.

— ***Conclusions:*** To explain the strong decrement of resistance to carbapenems in ICUs and GSCUs we hypothesized that there is not selective pressure for the establishment and maintenance of bacterial populations resistant to multiple antimicrobial compounds within this hospital, except for VSUs, where the selective pressure seems to be high.

— ***Keywords:*** Klebsiella pneumoniae, Carbapenemases, Carbapenemase, Klebsiella, Resistance, MDR.

INTRODUCTION

Klebsiella pneumoniae was firstly isolated in the late 19th century. Initially known as Friedlander's bacterium, it is the most important species of the genus *Klebsiella* in medicine[1]. It is a Gram-negative, encapsulated, nonmotile bacterium that resides in the environment, including soil and surface waters. It can also colonize human mucosal surfaces and the gastrointestinal tract where the effects of its colonization appear benign[2-5]. Carrier rates differ considerably within the various studies. The detection rate in stool samples ranges from 5 to 38%, while rates in the nasopharynx swabs vary from 1 to 6% in healthy people[6,7]. Detection rates are even higher in hospitalized patients: 77% of the stool samples and 19% of the pharynx swabs result positive[6,7]. This high

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rate of nosocomial *K. pneumoniae* colonization appears to be associated with the extensive use of antibiotics in a hospital setting. Sometimes, some *K. pneumoniae* strains can gain entry to other tissues and cause a wide range of severe infections. It is especially important in hospital-acquired infections, including severe pneumonia, urinary tract infection (UTI) as well as septicemia and wound infections[3,8,9-16,17-25]. *K. pneumoniae* is an extremely resilient bacterium and it owns the ability to evade and survive to the immune system; furthermore, several virulence factors have been demonstrated to mediate *K. pneumoniae* infectiousness and include adherence factors, capsule production, lipopolysaccharide presence, and siderophore activity[3,5,15,26-34]. *K. pneumoniae* is the second most common cause of gram-negative bloodstream infections (BSIs), after *Escherichia coli*, in adult population[22,35,36]. The increased use of antibiotics and persistent exposure of *K. pneumoniae* to antimicrobial agents facilitated the emergence of multidrug-resistant strains[37,38]. The emergence and global expansion of hypervirulent and multidrug-resistant (MDR) clones of *K. pneumoniae* have been increasingly reported in community-acquired and nosocomial infections[37,39-45]. The treatment of infections caused by *K. pneumoniae* has become more and more difficult as a result. Moreover, a wide range of antimicrobial resistance genes further restricts the available options to effectively treat infections. Known mechanisms of resistance include the production of β-lactamases such as extended-spectrum β-lactamases (ESBLs), cephalosporinases, and carbapenemases. The emergence and spread of carbapenem and cephalosporin resistant strains of *K. pneumoniae* are a considerable threat to public health. Because of the growing circulation of MDR *K. pneumoniae*, it is important to understand its epidemiology[17,18,46-64]. *K. pneumoniae* is a public health concern in Europe, more than one third of the isolates reported to by ECDC report inside to EARS-Net for 2016 were resistant to at least one of the antibiotic groups and combined resistance to multiple antibiotic groups was common. A smaller group of countries reported considerably higher levels of carbapenem. The vast majority of the carbapenem-resistant isolates had additional resistance to third-generation cephalosporins, fluoroquinolones and aminoglycosides. Some countries report emergence of resistance to colistin especially where there is a high-level of carbapenem resistance. However, as routine, colistin susceptibility testing offers some challenges[65-69]. Italy reports the second highest percentage (33.5%) of *K. pneumoniae* blood isolates resistant to the carbapenems in Europe, when compared to data published by the European Centre for Disease Control and Prevention (ECDC). ECDC reported that the proportion of *Klebsiella pneumoniae* blood isolates resistant to carbapenems increased from 1.3% in 2006 to 33.5% in 2015, whereas combined resistance (third-generation cephalosporin, fluoroquinolones and aminoglycosides) increased from 2.8% in 2005 to 29.7% in 2015[38,43,62,63,70].

The aim of this retrospective cross-sectional study was to evaluate the current situation and distribution of drug-resistant *K. pneumoniae* within the "G. Martino" University Hospital of Messina.

MATERIALS AND METHODS

We carried out a cross-sectional retrospective study collecting all the data about microbiological isolates of *Klebsiella pneumoniae* and their antimicrobial-resistances, considering all specimens and origins during a three years period (2015-2017). Vitek 2 automated system (bioMérieux, Italy) was used for isolate identification and antimicrobial susceptibility testing. Minimum inhibitory concentrations (MICs) were classified according to breakpoints established by the European Committee on Antimicrobial Susceptibility Testing (EUCAST 2018). We did not report about colistin, because broth microdiluition (BMD), the confirmation test as recommended by EUCAST, is not performed in our clinical microbiology laboratory. We focused our attention on the isolates possibly producing carbapenemases.

RESULTS

During 2015-2017, 1,563 non-duplicated strains of *K. pneumoniae* were isolated from different inpatients, specimen and wards in our hospital.

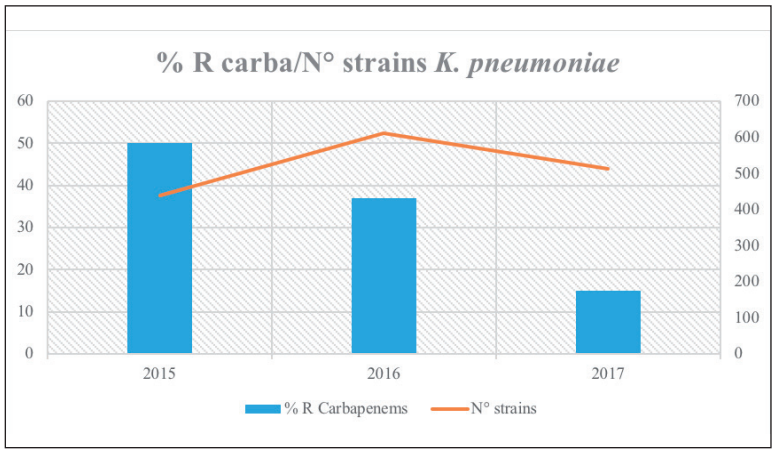

Figure 1. The graphic show the data decreased trend of the percentages of non-susceptible strains.

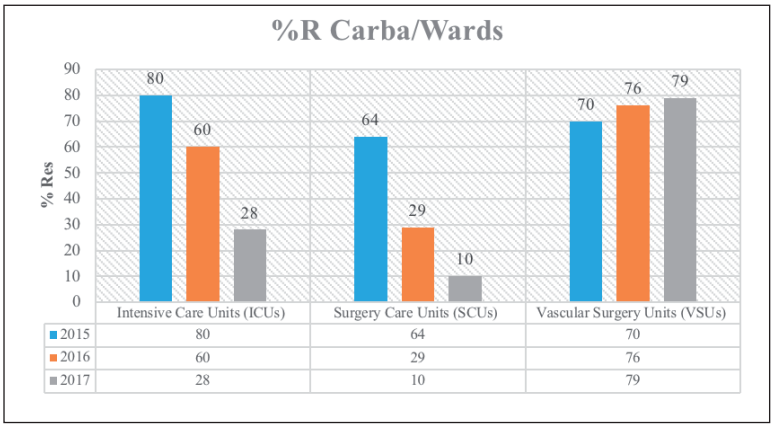

Figure 2. The graphic shows the data of resistances in our institution for different care units.

Among those strains, 523 (33,4%) were identified as non-susceptible (MIC >8) to meropenem and imipenem via Vitek 2 automated system (bioMérieux, Italy). We observed a strong decreased trend of the percentages of non-susceptible strains isolate between 2015 and 2017, namely 50% (218/439) in 2015, 37% (226/611) in 2016, 15% (79/513) in 2017 (Figure 1). We analyzed in detail the percentages of resistance in some high-risk departments, such as Intensive Care Units (ICUs), where resistance rates considerably decreased from the 80% of resistant strains found in 2015, to the 60% in 2016 and 28% in 2017; General Surgery Care Units (GSCUs), where the resistance strains decreased from the 64% found in 2015, to the 29% in 2016 and 10% in 2017 and Vascular Surgery Units (VSUs), where we assisted to an increase of resistance rates from the 70% found in 2015, to the 76% in 2016 and 79% in 2017 (Figure 2).

During the study period, we also observed a decrease in the occurrence of isolated of the *Klebsiella pneumoniae* from blood cultures. The analysis of the microbiological data revealed that in 2015 the *K. pneumoniae* isolates were 64 (12% of total positive blood cultures); in 2016 the *K. pneumoniae* isolates were 68 (10% of total positive blood cultures) and in 2017 the number of *K. pneumoniae* isolates was 55 (8% of total positive blood cultures), showing a decreasing trend during the study period. Table 1 resumes details about blood cultures, positive blood cultures and K. pneumoniae isolates during the period included in the study.

DISCUSSION

Gram-negative bacteremia is a major cause of morbidity and mortality if undiagnosed on time. β-lactam antibiotics, useful antimicrobial agents, play an important role in treating infection in the hospital population, in which, carbapenemases (CPMs) have the broadest spectrum and greatest stability against hydrolysis by β-lactamases[71]. Carbapenem-resistant *Klebsiella pneumoniae* (Kp-CPM) is currently one of the most important pathogens causing healthcare-associated infections, which typically occur in patients with prolonged hospital stay and previous antibiotic exposure. The most common mechanism of carbapenem resistance in *K. pneumoniae* is the production of carbapenemases[72-74]. CPMs have been regarded as a dependable drug for treating *K. pneumoniae* infections. However, with its increasing clinical usage, CPM-resistant *K. pneumoniae* are becoming more and more pervasive throughout the world. Our study describes the 3-year prevalence trend of CPM-resistant *K. pneumoniae* isolates responsible for infections in the wards of our hospital in Messina, Italy. Our study showed that the overall percentages of CPM-made *K. pneumoniae* decreased from 50% in 2015 to 15% in 2017 in our hospital. This decrease is in contrast with the European data for Italy processed by ECDC, these data show an increase to resistance (Figure 3).

CONCLUSIONS

To explain the strong decrement of resistance to carbapenems in ICUs and GSCUs we hypothesized that there is not selective pressure for the establishment and maintenance of bacterial populations resistant to multiple antimicrobial compounds within this hospital, except for VSUs, where the selective pressure seems to be high. To test this hypothesis, we will need more data about the antibiotics use in our hospital. However, studies about the antibiotics use are still on-going.

Table 1. Details about total blood cultures performed, positive blood cultures and *Klebsiella pneumoniae* isolates during the three years of the study

Years	Total blood cultures	Positive	Positive for *K. pneumoniae*	%
2015	2261	522	64	12
2016	2720	691	68	10
2017	2666	712	55	8

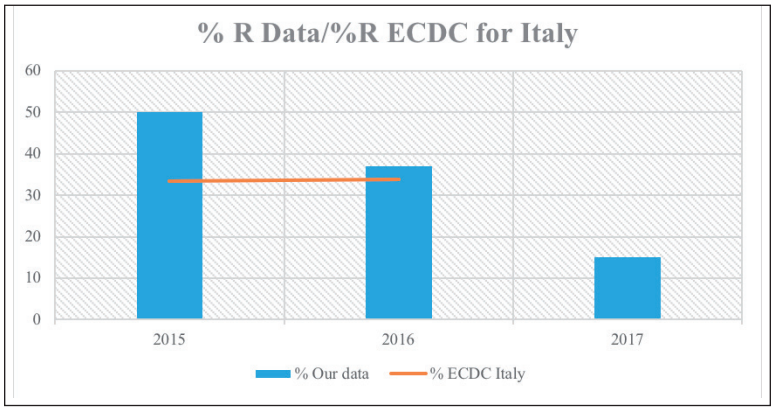

Figure 3. The graphic show the data of resistances in our institution compared with ECDC data for our country.

Conflict of Interest:
The Authors declare that they have no conflict of interests.

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