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Pseudomonas aeruginosa detection in South Italy: an epidemiological survey

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ABSTRACT:

— ***Objective:*** *Pseudomonas aeruginosa* is one of the principal causes of bacterial infections in healthcare and it represents a critical problem worldwide. Infections are becoming more difficult to treat because this bacterium is resistant to many commonly used antibiotics, including aminoglycosides, cephalosporins, fluoroquinolones and carbapenems. Drug resistance is associated with worse clinical outcomes: it facilitates prolonged hospitalization, multiple morbidities and increased health costs. The aim of this work was to evaluate the epidemiology of *Pseudomonas aeruginosa* during the years 2015-2017 in "G. Martino" University Hospital of Messina (Messina, Italy).

— ***Materials and Methods:*** We carried out an epidemiological study, collecting all the reports of *P. aeruginosa* isolates and relative resistances at the Microbiology Laboratory of the University Hospital "G. Martino" in Messina (Italy) during a three years period (2015-2017).

— ***Results:*** In our hospital, *Pseudomonas spp.* detection rates are equal to 14.6%, 12.3% and 13.3% of all microbial isolates in 2015, 2016 and 2017, respectively. During 2017, the Intensive Care Unit showed the highest mean percentages of *Pseudomonas spp*. detection (25%), followed by surgical area (18.4%) and medical area (22.2%). The percentages of resistance strains detection showed a decreasing trend in the considered period.

— ***Conclusions:*** Our study shows that, despite a decreasing trend during these three years period, P. aeruginosa infection still represents an important cause of healthcare-associated infections in our hospital. It is necessary to improve preventive measures to reduce the incidence of this infection.

— ***Keywords:*** Pseudomonas aeruginosa, Infection, Healthcare-Associated Infections, Antibiotic resistance, Epidemiology.

INTRODUCTION

Pseudomonas aeruginosa is an aerobic gram-negative bacterium and one of the most common nosocomial pathogens[1]. It is ubiquitous in many different environmental settings such as water, soil and plants[2]. The blue-green coloration produced during culture is a peculiar characteristic from which its name derives: in 1869 Fordos first identified the cause of this coloration, extracting the blue pigment called "pyocyanin". In 1882, Carle Gessard described the growth of the bacterium from cutaneous wounds of two patients with blue-green pus[3]. *P. aeruginosa* is involved in a variety of nosocomial infections including hospital-acquired pneumonia (HAP), urinary tract infections and central line-associated bloodstream infection. Urinary tract infections are the most common, lower respiratory tract and bloodstream infections are the most lethal[4]. It is also the most important cause of chronic lung infections contributing to the mortality of patients with cystic fibrosis[5]. Risk

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factors for *P. aeruginosa* infection include impairment of the immune system, prolonged hospitalization, prolonged antimicrobial therapy, and mechanical ventilation. Patients who underwent organ transplantation, invasive procedures (such as tracheostomy) or immunosuppressive therapy, patients with catheters or subjected to surgical intervention are more susceptible to infection, causing higher morbidity and mortality among them[6]. Transmission through contaminated medical devices, healthcare workers' hands and patient-to-patient transmission represent a well-established mechanism of its spreading. Moreover, the persistence of *P. aeruginosa* is facilitated by hospital reservoirs such as breathing and hemodialysis devices, sinks, water, bathrooms, surfaces[7-10].

P. aeruginosa represents a critical problem and a challenge in medical practice worldwide: infections are becoming more difficult to treat because this bacterium is resistant to many commonly used antibiotics, including aminoglycosides, cephalosporins, fluoroquinolones and carbapenems[11]. Drug resistance is associated with worse clinical outcomes: it facilitates prolonged hospitalization, multiple morbidities and increased health costs[12-15]. This pathogen is not only intrinsically resistant to a wide range of antimicrobials, but it is also capable to develop resistance to commonly used antimicrobials through acquired mutations in chromosomal genes[16-18]. Intrinsic drug resistance is mainly due to low outer membrane permeability, the expression of efflux pumps and the production of enzymes conferring resistance to β-lactam and aminoglycoside antibiotics[19-25]. Antibiotics including β-Lactams, aminoglycosides, fluoroquinolones and carbapenems can enter cells by diffusing through porins of the outer membrane[22,23]. P. aeruginosa limits antibiotic entry acting on the outer membrane permeability, reducing the number of non-specific porins and replacing them with specific or more-selective channels[25]. The outer membrane of *Pseudomonas*, thus, becomes an effective barrier to the mentioned antibiotics. Reduction in drug accumulation can also be achieved through active export by membrane-associated pumps. Efflux pumps confer resistance to different antibiotics: MexAB-OprM and MexXY-OprM confer resistance to fluoroquinolones, aminoglycosides, tetracyclines and β-lactams. MexAB-OprM also confers resistance to meropenem (but not imipenem) and MeXY-OprM acts against cefepime but not ceftazidime[19,26,27]. At last, *P. aeruginosa* produces an AmpC-like inducible chromosomal b-lactamase that can inactivate b-lactams: AmpC overproduction can lead to an increased resistance[20,21]. Acquired resistance genes are mostly involved in resistance to b-lactams, aminoglycosides and carbapenems: strains able to product extended-spectrum βlactamases (ESBL) and metallo-β-lactamases have spread worldwide[28]. Intensive Units Care are the settings where outbreaks are more often registered[29,30]. European surveillance data[31] show significantly decreasing trends in resistance for *P.aeruginosa* for all antimicrobial groups under surveillance during the period 2014 to 2017. High resistance percentages persist in many countries, especially in the Eastern and South-Eastern parts of Europe. The highest mean resistance percentage in 2017 was reported for fluoroquinolones (20.3%), followed by piperacillin ± tazobactam (18.3%), carbapenems (17.4%), ceftazidime (14.7%) and aminoglycosides (13.2%) (Table I). In Table II, the Italian situation is presented: also, in this case the highest mean resistance percentage in 2017 is described for fluoroquinolones (25.1%), followed by piperacillin ± tazobactam (24.2%), ceftazidime (20%), carbapenems (19.9%) and aminoglycosides (18%). The aim of this retrospective cross-sectional study is to evaluate the prevalence of resistant strains of *P. aeruginosa* in the University Hospital "G. Martino" of Messina (Messina, Italy) and compare our epidemiological situation with the national and international ones.

Table 1. Revised from ECDC, 2018. Percentages of resistance to antibiotics in Europe (2015-2017)[31].

	2015	2016	2017
Piperacilline/Tazobactam	19.9%	18.8%	18.3%
Fluoroquinolones	20.9%	18.8%	20.3%
Ceftazidime	15.4%	14.4%	14.7%
Aminoglycosides	15.3%	14.1%	13.2%
Carbapenems	19.4%	18.2%	17.4%

MATERIALS AND METHODS

We carried out a cross-sectional study collecting anti-microbial-resistances of *P. aeruginosa* isolated in the Messina University Hospital "G. Martino" during the three years period 2015-2017. The data were provided by the Local Microbiology Laboratory. Anti-microbial susceptibility tests were obtained using Vitek 2.0 automatic system (Biomerieux, Florence, Italy). Data were analyzed with descriptive statistics (mean, percentage, standard deviation).

RESULTS

In the considered three years period, in our hospital, we observed *Pseudomonas spp.* detection rates amounting to 14.6%, 12.3% and 13.3% of all microbial isolates in 2015, 2016 and 2017, respectively. The percentages of its

Table 2. Revised from ECDC, 2018. Percentages of resistance to antibiotics in Italy (2015-2017)[31].

	2015	2016	2017
Piperacilline/Tazobactam	29.5%	30.7%	24.2%
Fluoroquinolones	24.6%	24.7%	25.1%
Ceftazidime	21.7%	23%	20%
Aminoglycosides	17.2%	19.1%	18%
Carbapenems	23%	23.5%	19.9%

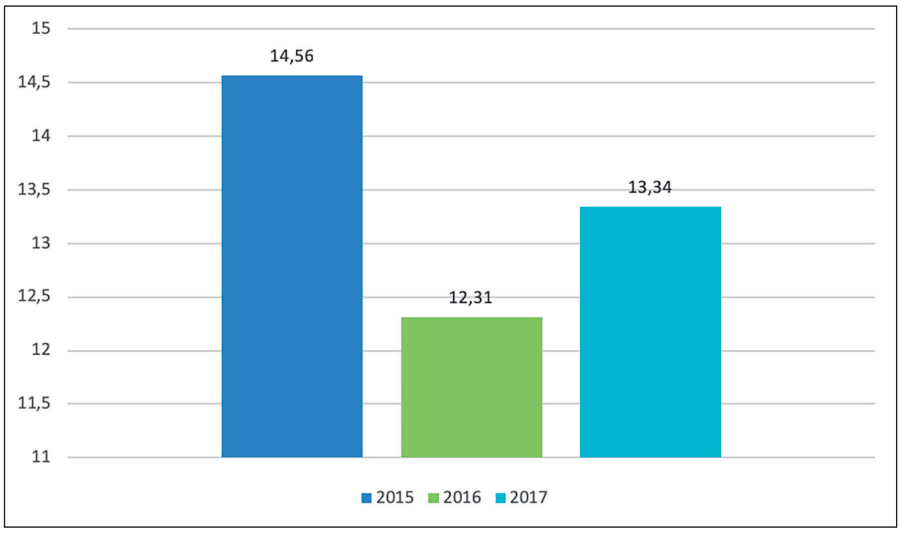

Figure 1. Percentages of P. aeruginosa detection rates isolated in all the Hospital in the three years period 2015-2017.

detection compared to all the microbial isolates in all the entire hospital are shown in Figure 1. The percentages of *Pseudomonas aeruginosa* detection in the Hospital wards in 2015, 2016 and 2017 are shown in Table III. Fibrosis cystic ward always showed the highest percentages of *P. aeruginosa* detection, followed by Pediatric ICU. In 2017, emergency area showed the highest mean percentages of *P. aeruginosa* detection (25%), followed by surgical area (18.4%) and medical area (22.2%). During the study period, we also observed the occurrence of isolated of *P. aeruginosa* from blood cultures. Our data show that in 2015 the *P. aeruginosa* isolates represented the 3.6% of total positive blood cultures; in 2016 the isolates were the 2.7% of total positive blood cultures and in 2017 the 3.6% of total positive blood cultures (Table IV).

We then evaluated the rate of detection of resistance strains. Figure 2 shows the percentages of resistance to ceftazidime, piperacilline/tazobactam, fluoroquinolones, aminoglycosides and carbapenems. As it can be observed from the figure, the percentages of resistance strains detection showed a decreasing trend in the considered period.

Table 3. Percentages of *PA* detection in the various wards of the three considered areas.

	2015	2016	2017
Surgical Area			
General Surgery	23	10	12.5
Oncological Surgery	14.6	8.1	11.6
Neurosurgery	13.2	14	25.5
Pediatric surgery	25.5	15	27.8
Plastic Surgery	7.7	28.6	15.5
Thoracic Surgery	27.2	23.5	17.5
Vascular Surgery	25.8	20.9	21.3
Orthopaedics	35.4	27	15.2
Medical Area			
Gastroenterology/ Cystic Fibrosis	83	74	78.6
Geriatrics	16	17.1	22
Infectious diseases	27.7	34.7	12.1
Internal Medicine	15	14.2	17.2
Nephrology	13.3	13.1	10
Neurology	25	5.8	11
Pulmunology	12.2	26	22
Oncology	23.1	3	5
Emergency Area			
Pediatric ICU	66	38.2	41
Cardiological ICU	28.7	28.6	17.7
Adult ICU	16.6	14.3	16.4

DISCUSSION

Antimicrobial resistance is recognized as a major public health burden worldwide[32,33]. Multidrug-resistant (MDR) *P. aeruginosa* is associated with worse outcomes, higher mortality and increased health costs[5,12,16,34,35]. In our hospital we observed a decrease of *P. aeruginosa* detection, with a percentage of 13.3% in 2017 (Figure 1). Our study showed that the overall percentages of resistance to antibiotics decreased during these three years period in our hospital, in line with European and Italian data processed by ECDC[31] (Table I-III). Control of *Pseudomonas* infections requires strategies for risk factors early identification, detection of resistant organisms and implementation of prevention strategies. Several studies[7,12,36-40] show the importance of *Pseudomonas* transmission between patients by healthcare workers (HCWs)'s hands: hand hygiene using alcohol-based products is one of the most helpful and, at the same time, simplest practice to reduce *P. aeruginosa* and MDRs pathogens spread. Training courses for doctors, nurses, cleaning staff are needed to reach a greater awareness: use of alcohol-based products, disposable gowns and gloves and patient's isolation in a single room are three of the main recommendations to control the transmission. Healthcare environment is a *Pseudomonas* reservoir: its early identification and its subsequent decontamination are another way to control its spreading. Infection control practices must involve all the hospital departments, mainly focusing on the most critical.

Table 4. Details about positive blood cultures and *P. aeruginosa* isolates during the three years of the study.

Years	Positive blood cultures	Positive for *P. aeruginosa*
2015	23%	3.6%
2016	25.4%	2.7%
2017	26.7%	3.6%

Table 5. Percentages of resistance to antibiotics in "G.Martino" Hospital (2015-2017).

	2015	2016	2017
Piperacilline/Tazobactam	33%	22%	1%
Fluoroquinolones	18%	17%	3%
Ceftazidime	22%	30%	5%
Aminoglycosides	11%	10%	4%
Carbapenems	20%	15%	5%

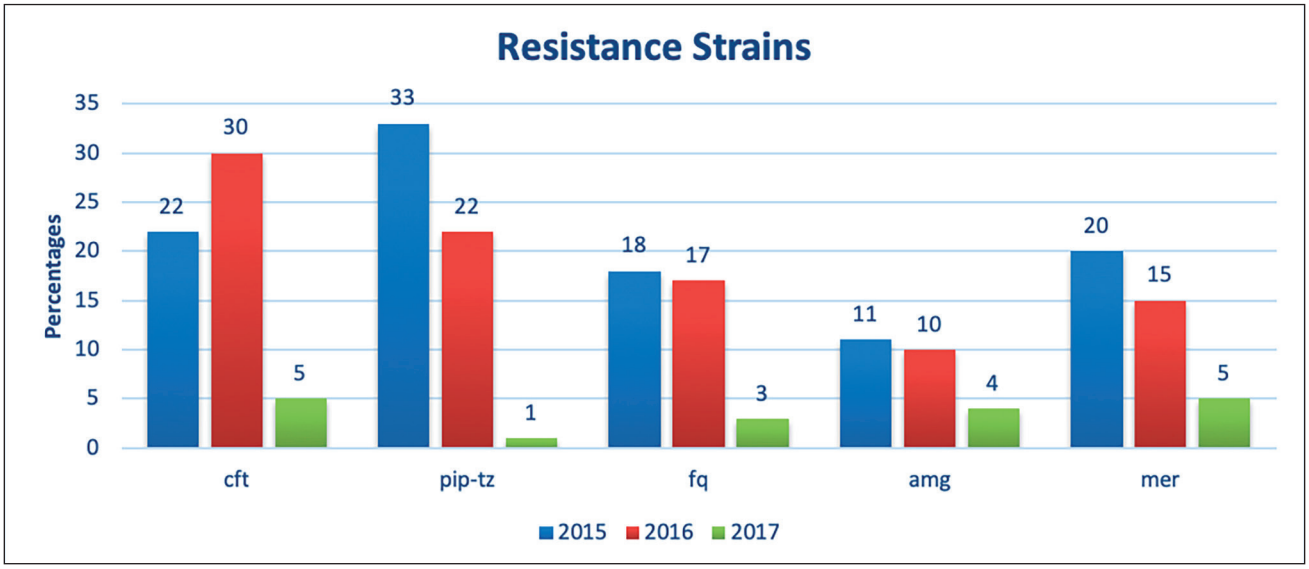

Figure 2. Resistance strains detection during 2015-2017.

CONCLUSIONS

Pseudomonas aeruginosa continues to be an important public health issue in our hospital and a cause of nosocomial infections. Optimisation of preventive measures to reduce this burden is still needed.

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

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